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# CONTENTS

April / June 2011

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**Brazilian Journal of Videoendoscopic Surgery**

*Editorial*

# Systematic Reviews and Meta-Analysis of Therapeutic Interventions: How to Better Understand Them?

## Revisão Sistemática e Metanálise de Intervenções Terapêuticas: Como Melhor Entendê-las?

**RAPHAEL CÂMARA MEDEIROS PARENTE[1]; EVANDRO DA SILVA FREIRE COUTINHO[2]; MARCO AURÉLIO PINHO DE OLIVEIRA[3]; ROGER KELLER CELESTE[4]; PAULA DE HOLANDA MENDES[5]; RICARDO BASSIL LASMAR[6]**

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**ABSTRACT**

In the past decade, the Era of Evidence-Based Medicine, the number of meta-analysis dramatically increased. Meta-analyses statistically combine the results of multiple studies and are considered to be the highest level of evidence when the results of high-quality randomized trials are combined in an appropriate way. Results from a meta-analysis may not correspond to reality because of the large variation in the quality of the studies that have been pooled, and clinical and methodological differences among the included studies. The growing popularity of systematic reviews and meta-analyses has made it important to better understand them. The objective of this article is to help the reader comprehend how a systematic review and meta-analysis is carried out and to be better able to interpret them. We explain some impor tant aspects of conducting a meta-analysis. A better understanding of the basic terminology and the concepts involved in generating a systematic review and meta-analysis may help the clinician better evaluate the quality of a meta-analysis and the real importance of its findings for a specific patient.

**Key words:** Meta-analysis, Systematic Review, Clinical Trial.

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## INTRODUCTION

Evidence-Based Medicine (EBM) is the systematic process of searching, quality assessment, and the application of recent research results as a basis for clinical decisions.[1] Systematic reviews seek to present – in a critical and integrated way – the results of existing studies. Using a clear and objective process to search for and evaluate existing research on a given subject, the best available evidence is obtained for clinical decision-making. As a result, it is not surprising that the number of systematic reviews and meta-analysis has been growing in significant ways since the 1990s. A Medline search showed that this technique of reviewing the literature increased 20-fold between 1989 and 1991 (*Marco – check this, a two year interval doesn't seem correct. It seems like the period of comparison should be longer to see a 20 fold increase, unless the initial base was miniscule.)* The change in philosophy brought about by evidence-based medicine, combined with growth in scientific output in the biomedical area, certainly was major factor in this increase. Whereas in 1940 there were about 2,300 biomedical journals, 50 years later this number soared to nearly 25,000.[2] These data give an idea of the problem faced by health professionals to assimilate the knowledge generated and make decisions based on that knowledge.

## SYSTEMATIC REVIEW

There are several ways of dealing with this vast bibliography. One of them is using "narrative reviews". Narrative review, however, usually have different goals than systematic reviews. Narrative reviews are broad in terms of content, may express personal opinions and commentaries about the state of the art, selecting studies in a subjective manner, without clear criteria. The style of these reviews is characterized by sequences/series of "who said what?" permeated by a bibliography. The lack of objective criteria and limited integration of findings may lead to erroneous conclusions, if the purpose of such reviews was to provide a summary of all existing literature on the topic.

In contrast, systematic reviews, have as their focus responding to a specific clinical question. Systematic reviews require a search for studies using selective criteria, analysis of the quality of the studies selected, assessment of differences between the results of different studies, and the synthesis of the results of the studies in a qualitative way in the case of the systematic review and in a quantitative way in the case of the meta-analysis, as will be explained later. A systematic review is called a meta-analysis when statistical techniques are used to combine the data of different studies.

Systematic reviews and meta-analyses have their origins in astronomy, proceeding through agriculture, education, whose methods of numerical synthesis of results were developed by statisticians such as R.A. Fisher, L. Tippett, K. Pearson, E.S. Pearson, F. Yates, and W. G. Cochran.[2] Already in the early twentieth century Karl Pearson had published a synthesis of results of studies about the effectiveness of the vaccine against typhoid fever in soldiers, meta-analysis only gained expression in the medical field starting with the study of Thomas Chalmers and Joseph Lau, on the efficacy of streptokinase in reducing the mortality of patients with acute myocardial infarction. This trend got a boost with the creation, in 1992, of the Cochrane Centre at Oxford University, in England, in order to prepare, maintain and disseminate systematic reviews of controlled clinical trials.

### Stages of a systematic review

Any systematic review and meta-analysis should be preceded by a protocol in which the strategy to be used must be specified. The steps of a systematic review and meta-analysis are shown in Figure 1. Clearly formulated questions, along with clear criteria for inclusion and exclusion of studies are essential to the process of identifying relevant studies for review and meta-analysis. It is necessary to have clarity about the characteristics of the population for whom the answer the original question is intended, the exposure that you want to investigate, as well as the clinical outcome that one wants to measure. It should also define what types of studies will be included (e.g. controlled clinical trials, case-control studies, cohort studies). Ideally, a systematic review of therapeutic or preventive procedures should include only randomized controlled trials.

**Question:** Objective and operationalized in order to be tested.

Ex: Does hormone therapy improves osteopenia in postmenopausal women?

**Participants:** Characterize the population regarding gender, age, clinical characteristics (if applicable). For example, women in the immediate postmenopausal period, regardless of social background, without osteoporosis. Define the degree of osteoporosis permitted in the study.

**Intervention:** Specify any hormone or one specific type.

**Outcome:** Specify how the improvement of osteopenia will be is defined and measured.

**Type of study:** For example, only randomized controlled trials.

This is followed by the phase in which relevant studies are identified. Restricting the search to Medline can lead to the distortions in the results of the systematic review, depending on the topic that you want to investigate. There are several databases of research studies for specific problems such as cancer, non-pharmacological care of the mentally ill, post-traumatic stress disorders, to cite a few examples. On the other hand, it is known that studies with negative results are less likely to be published, especially in major indexed journals; this can lead to an error called publication bias. In the case of therapeutic interventions, publication bias leads to the identification of nonexistent efficacies or exaggerates the magnitude of this efficacy.

One way to minimize the risk of this bias is to expand the search to non-indexed journals and conference proceedings, consulta experts, and search sites that register clinical trials, such as those present at www.york.ac.uk /inst/crd/revs.htm.

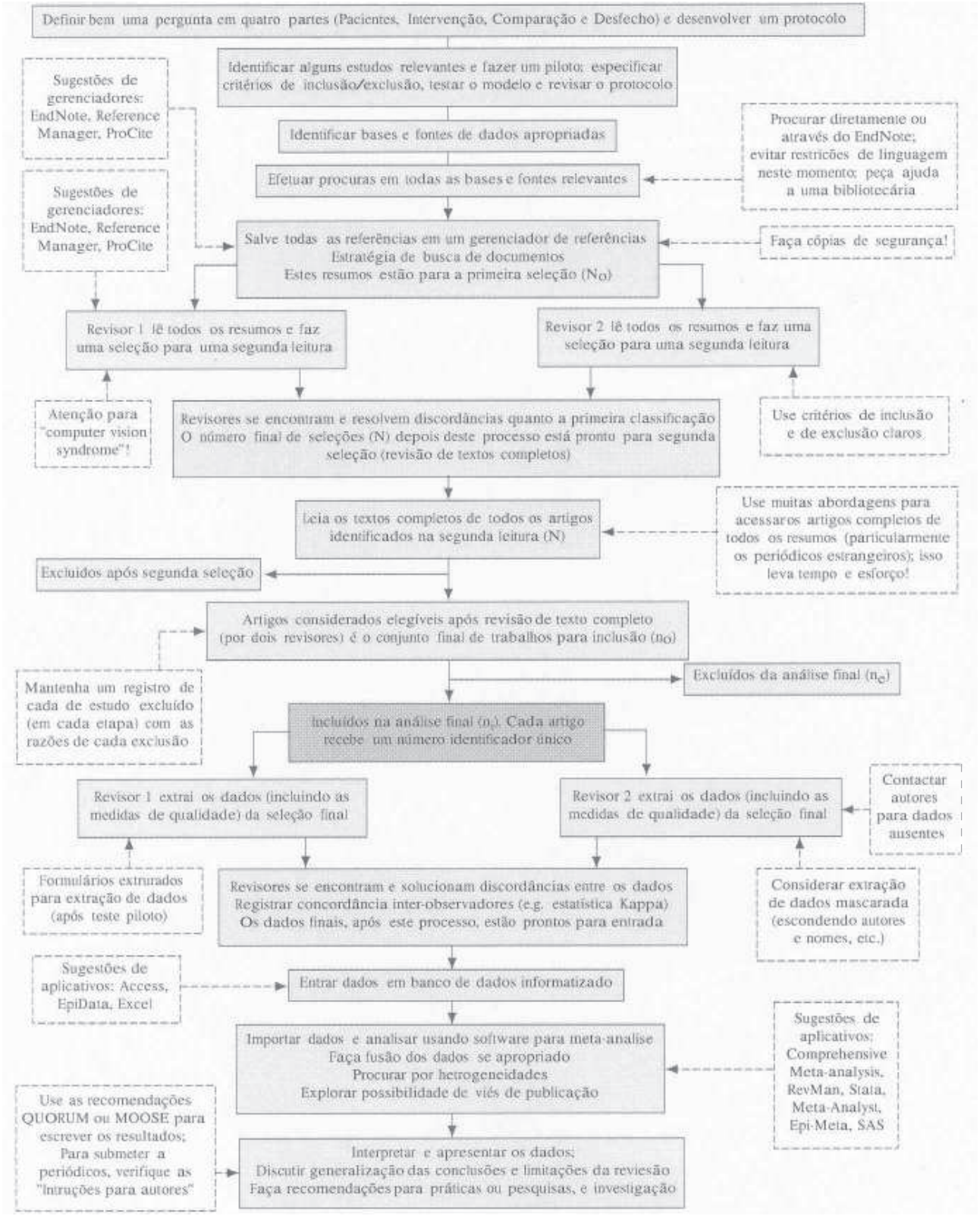


***Figure 1*** *- Stages of a systematic review.*
*Madhukar Pai, Michael McCulloch, and Jack Colford. Systematic Reviews Group, UC Berkeley, 2002 [madhupai@uclink.berkeley.edu]*
*Translated from Portuguese by: Peter Emmanuel A. A. do Brazil, Master's candidate - IMS / UERJ, 2004 (pemmanuel@ig.com.br)*
*Available at: http://www.medepi.net/meta/guidelines/Berkeley_Systematic_Reviews_Road_ Map_V22_Versao_Brasileira.pdf*

Another important error to avoid is the exclusion of articles written in less common languages. It is known that studies that report favorable results for the tested interventions tend to be published in English. So even if one cannot translate articles published, for example, in German or Japanese, they should be identified in the search so that later one can assess the possible impact of their exclusion on the findings of the systematic review.

Once the search is concluded, the study selection process begins with the evaluation of the titles and abstracts, to see if the articles meet inclusion criteria. In this step it is important, although difficult, that the evaluators are masked ("blind") regarding the origin of the work. This because, there is a chance that an article might be included or excluded solely because the evaluator already knows the group that published it or because the work was published in a particular journal. Having two researchers read each abstract may reduce the chance that an article of interest will be overlooked. Next, complete copies of the articles that meet the criteria or for which there is doubt about the relevance to the review are obtained. Articles can still be excluded at this stage, but the reason for this decision should be noted. The selection process should be documented, preferably in a flowchart. Figure 2 presents the model proposed by the "Quality of Reporting of Meta-Analysis Group – **QUOROM**,"[3] with documentation of how many studies were excluded at each step of the selection and the reason for these exclusions. In the case of observational studies, a proposal for a similar presentation of point was made by "Meta-analysis Of Observational Studies in Epidemiology Group-**MOOSE**". [4]

The selected studies should be evaluated regarding their **methodological quality** according to criteria established in the Protocol. A list of 22 criteria used to describe the quality of randomized clinical trials is described by the Consolidated Standards of Reporting Trials Group - CONSORT".[5] It is suggested that two researchers are involved in this phase, as well as in a later stage - the **extraction of information**.

## META-ANALYSIS: QUANTITATIVE SYNTHESIS OF RESULTS

### Summary-Measures and Forest Plot

If the studies are homogeneous, one can combine their results in a summary-measure. This measure

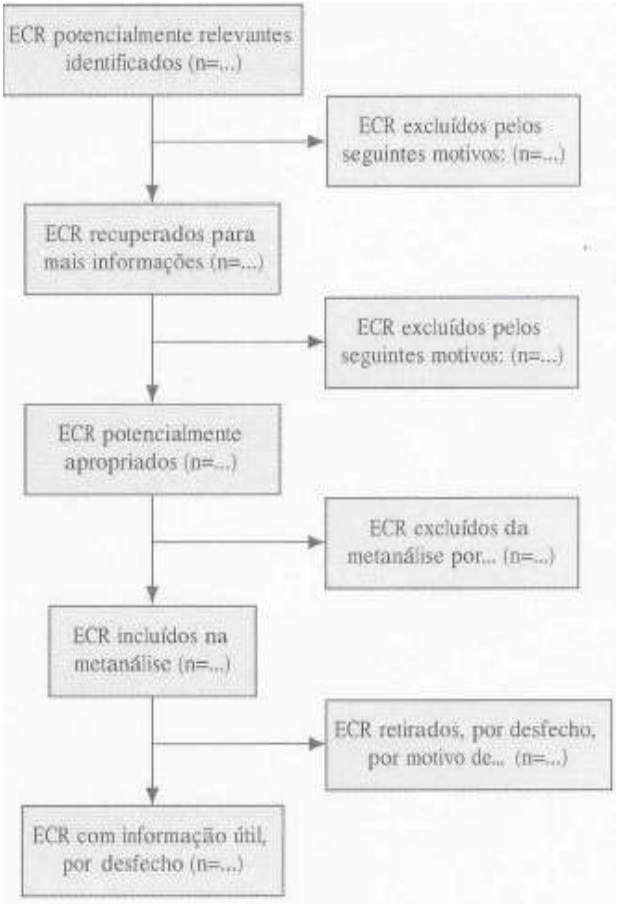


***Figure 2** - Flowchart with the stages of a meta-analysis of clinical trials, proposed by the QUOROM (3).*

increases the statistical power[a] and precision of the estimates, by increasing the sample size attained by combining several studies. Statistical techniques, however, are not able to correct biases in the review process. If the raw material is not of good quality, the result is not valid.

The summary-measure is obtained from a weighted average of the results of several studies, in which the weights are the inverse and their variances. In other words, studies with more precision (due to a larger sample size) are given more weight in the combined estimate. One of the statistical methods most commonly used for this purpose is the Mantel-Haenszel.

In Figure 3 we constructed a graph (forest plot) with data from a meta-analysis conducted by

[a] *Capacity of the statistical test to detect an effect of the intervention when it differs from the control group.*

Roberts and Dalziel[6] about the effectiveness of corticosteroids for accelerating fetal lung maturation in women at risk of giving birth early/prematurely. With minor variations, these graphs contain the following two elements:

1) Each line represents one study, the estimated relative risk (RR)[b] conveyed by a small square. The horizontal line that bisects the square is the 95% confidence interval.[c] One observes that in 13 of the 18 studies, the confidence interval includes the null value (relative risk = 1); such studies considered inconclusive.

2) The small diamond at the bottom represents the summary-measure. In the example in Figure 3, the combined relative risk (RR) was 0.69, which means a reduction (efficacy) of 31% [d] in the risk of neonatal death in the group in which mothers had used corticosteroids, compared with the control group. The 95% confidence interval of this RR (0.58 to 0.81, p <0.01) does not include the null value. It can be concluded that the prenatal use of corticosteroids during pregnancy reduces the risk of premature birth by 31%, and the probability that this finding is due to chance is less than 5%.

The squares indicating the RR of each study vary in size, and the weight accorded to each study to estimate the pooled RR is proportional to each square's area. The relative weight of each study appears in the right column of the chart.

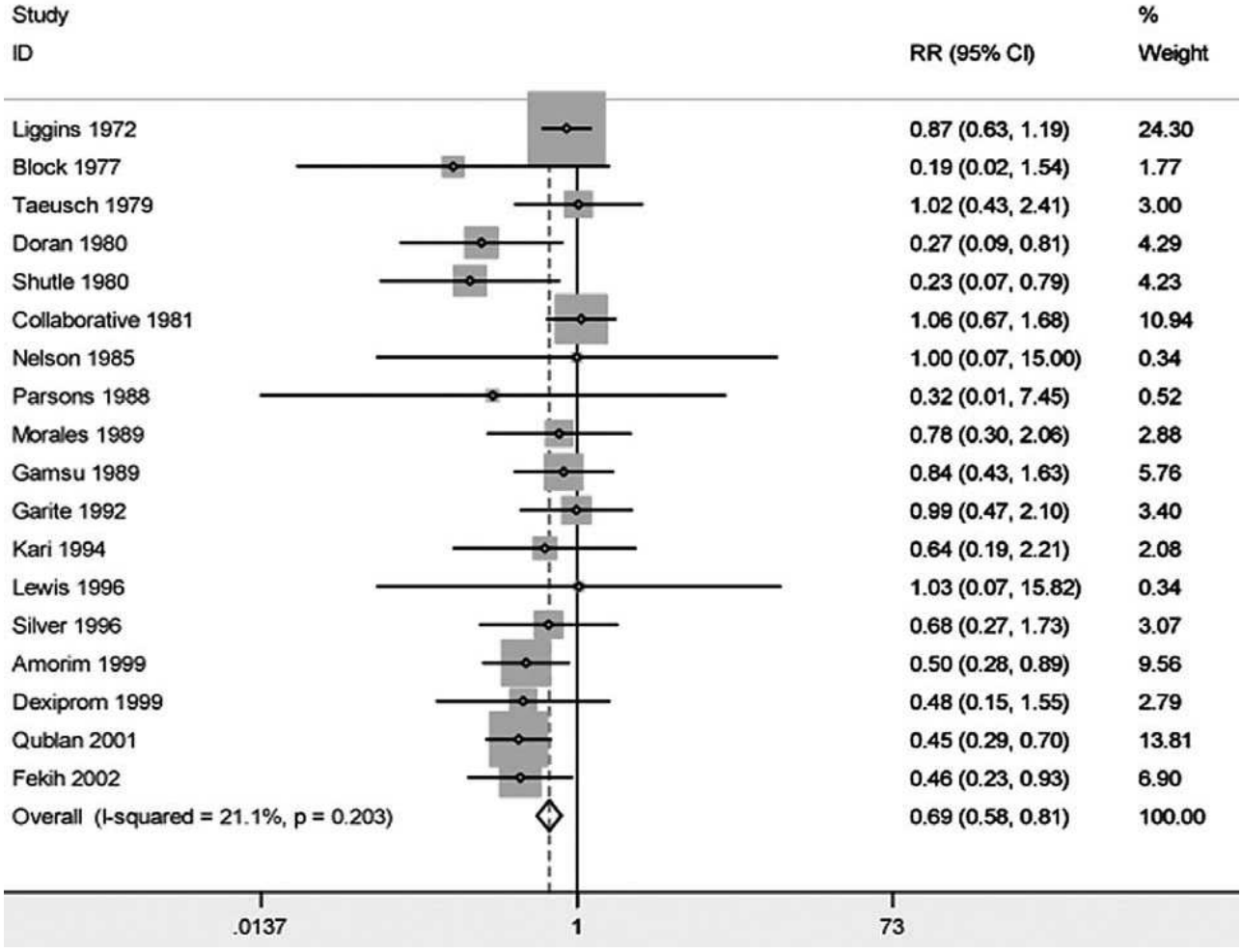


***Figure 3 -*** *Forest plot of clinical trials comparing the relative risks for neonatal mortality of premature infants in pregnant women who used corticosteroids or received a placebo. Graph produced with the command "metan" (fixed effects) of Stata statistical package, version 9.0, from raw data presented by Roberts and Dalziel.*[6]

*[b] Risk of neonatal death in the group of mothers who received corticosteroids divided by the risk of neonatal death in the group of mothers who received placebo. The RR is equal to 1 when there is no difference between the two groups being compared.*

*[c] Range of values that includes, with 95% confidence, the value of RR if all individuals, and not just a sample, had they been studied.*

*[d] Efficiency = (1 – 0.69) x 100.*

**Evaluating the heterogeneity**

It is common for the selected studies to have findings/results that are inconsistent. The fact that the difference between them exceeds what would be expected by chance is defined as statistical heterogeneity. Such heterogeneity reflects distinctions between studies, with regard to aspects of design, that included differences in the population studied, in the way the intervention or outcome is measured, the methodological quality of studies, among others.[4] In this case, it does not make sense to obtain only a summary measure, but one should explore the reasons for this inconsistency.

Thompson[7] exemplifies this situation with studies about the effect of endoscopic sclerotherapy of esophageal varices on the reduction of the mortality in patients with hepatic cirrhosis, and the efficacy of the reduction of serum cholesterol on the mortality from ischemic heart disease. In the case of the first meta-analysis, the heterogeneity of the results can be attributed to differences between the studies regarding the severity of underlying disease (cirrhosis), the endoscopic technique used (intervention), the management of complications, and length of follow-up of the patients.

Two strategies for investigating the factors related to heterogeneity are: subgroup analysis and meta-regression. In case of the former, the studies are subdivided into levels for the variable that is believed to be causing the heterogeneity. In the case of endoscopic sclerotherapy, the studies could be analyzed separately according to severity of underlying disease, to form more homogeneous groups. This procedure requires a large number of studies.

Meta-regression is a generalization of the subgroup analysis, which examines the relationship between levels of a characteristic of the study (e.g., duration, dose, disease severity, average age of the group) and the variation in the measure of effect (e.g., risk relative, risk difference, difference of means) of the studies.[7] Its implementation requires one makes use of multivariate models, which is beyond the scope of this article.

## FINAL THOUGHTS/CONSIDERATIONS

Although the meta-analysis of clinical trials has reached a high degree of acceptance in the clinical and statistical literature, some authors have been critical about its use in general or, more specifically, when applied to non-experimental studies. A careful reading of these articles reveals that much of the criticism is focused on methodological aspects inherent to the designs of the studies upon which the meta-analysis is constructed, including violations of the basic methodological principles or methodological procedures considered unsuitable for meta-analysis. For example, it is not correct to say that the meta-analysis does not consider the quality of studies or the heterogeneity among their findings, mixing "apples and oranges." The quality is often considered both in the process of the inclusion/exclusion of studies and in the evaluation of their possible impact on the conclusion.

As for heterogeneity, several articles on meta-analysis have drawn attention to the need to seek explanations for the inconsistencies among studies and not calculate summary-measures by combining heterogeneous results. For Liberati,[8] this type of criticism stems from a distorted view that considers meta-analysis a simple statistical combination of data.

All the foregoing does not exempt meta-analysis of a series of problems. Because of the fact that it always done after the data have been collected, it is susceptible to hindsight biases of retrospective research. It is common for meta-analysis on the same subject are different results.

Despite the criticism, meta-analysis has been considered by many authors one of the most important innovations in the methodology of clinical research. More recent movements have incorporated the knowledge produced by systematic review and meta-analysis. This is the case of evidence-based medicine and, more recently, evidence-based public health. It is in this context that Liberati [8,9] reminds the critics of this methodology that the only alternative to systematic reviews is to perform non-systematic reviews, whose subjectivity and lack of well-defined criteria are a breeding ground for conclusions of little practical application, or even wrong .

**RESUMO**

Na última década, Era da Medicina Baseada em Evidências, o número de metanálises cresceu significativamente. A metanálise combina estatisticamente os resultados de vários estudos e estes são considerados o mais alto nível de evidência quando são combinados de forma apropriada os resultados de ensaios clínicos metodologicamente bem conduzidos. Resultados de uma metanálise podem não corresponder à realidade, pelo fato de depender da qualidade dos estudos nela inseridos, além de diferenças clínicas e metodológicas entre os estudos incluídos. A crescente popularidade de metanálises e de revisões sistemáticas faz com que seja necessário melhor compreendê-las. O objetivo deste artigo é fazer com que o leitor entenda como é realizada uma metanálise/revisão sistemática e que tenha melhores condições de interpretá-la. A melhor compreensão da terminologia adotada e dos conceitos envolvidos na sua produção pode ajudar o clínico a avaliar melhor a qualidade de uma metanálise e a real importância de seus resultados para um paciente específico.

**Palavras-chave:** Metanálise / Revisão Sistemática Ensaio Clínico.

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**Brazilian Journal of Videoendoscopic Surgery**

*Editorial*

# Revisão Sistemática e Metanálise de Intervenções Terapêuticas: Como Melhor Entendê-las

## Systematic Reviews and Meta-Analysis of Therapeutic Interventions: How to Better Understand Them?

**RAPHAEL CÂMARA MEDEIROS PARENTE[1]; EVANDRO DA SILVA FREIRE COUTINHO[2]; MARCO AURÉLIO PINHO DE OLIVEIRA[3]; ROGER KELLER CELESTE[4]; PAULA DE HOLANDA MENDES[5]; RICARDO BASSIL LASMAR[6]**

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**RESUMO**

Na última década, Era da Medicina Baseada em Evidências, o número de metanálises cresceu significativamente. A metanálise combina estatisticamente os resultados de vários estudos e estes são considerados o mais alto nível de evidência quando são combinados de forma apropriada os resultados de ensaios clínicos metodologicamente bem conduzidos. Resultados de uma metanálise podem não corresponder à realidade, pelo fato de depender da qualidade dos estudos nela inseridos, além de diferenças clínicas e metodológicas entre os estudos incluídos. A crescente popularidade de metanálises e de revisões sistemáticas faz com que seja necessário melhor compreendê-las. O objetivo deste artigo é fazer com que o leitor entenda como é realizada uma metanálise/revisão sistemática e que tenha melhores condições de interpretá-la. A melhor compreensão da terminologia adotada e dos conceitos envolvidos na sua produção pode ajudar o clínico a avaliar melhor a qualidade de uma metanálise e a real importância de seus resultados para um paciente específico.

**Palavras-chave:** Metanálise / Revisão Sistemática Ensaio Clínico.

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## INTRODUÇÃO

Medicina baseada em evidências é o processo sistemático de busca, avaliação da qualidade e aplicação dos resultados de pesquisas recentes, como base para decisões clínicas1. Revisões sistemáticas buscam apresentar, de forma crítica e integrada, os resultados dos estudos existentes, obtidos de um processo claro e objetivo de busca e avaliação de pesquisas existentes sobre um dado tema; portanto, são a melhor evidência existente para tomada de decisões clínicas. Em virtude disso, não é surpreendente que o número de revisões sistemáticas e de metanálises venha crescendo de modo importante a partir da década de 1990. Uma pesquisa no *Medline* mostrou que esta técnica cresceu 20 vezes entre 1989 e 1991. A mudança de filosofia trazida pela medicina baseada em evidências, aliada ao crescimento da produção na área biomédica, contribuiu de forma decisiva para esse aumento. Se em 1940 havia cerca de 2.300 revistas biomédicas, 50 anos depois esse número subiu para quase 25.0002. Esses dados dão idéia do problema enfrentado pelos profissionais de saúde para acompanhar o conhecimento produzido e tomar decisões com base nesse conhecimento.

## REVISÃO SISTEMÁTICA

Existem várias formas de se lidar com essa vasta bibliografia. Uma delas é a partir de revisões

narrativas. Entretanto, elas costumam ter objetivos diferentes das revisões sistemáticas. As revisões narrativas são amplas em termos de conteúdos, expressam opiniões pessoais e comentários sobre o estado da arte, selecionando estudos de forma subjetiva, sem critérios claros. O estilo dessas revisões caracteriza-se por seqüências de "quem disse o que?", permeadas por uma bibliografia. A falta de critérios objetivos e a pouca integração dos resultados podem levar a conclusões equivocadas, se o objetivo de tais revisões for realizar um resumo de toda literatura existente.

Revisões sistemáticas, ao contrário, têm como foco a resposta de uma questão clínica específica, requerem a busca de estudos com seleção criteriosa, análise da qualidade dos estudos selecionados, avaliação de diferenças entre resultados de diferentes estudos e a síntese do resultado dos estudos de forma qualitativa no caso da revisão sistemática e quantitativa no caso da metanálise, como será explicitado adiante. Uma revisão sistemática é chamada de metanálise quando faz uso de técnicas estatísticas para combinar os dados dos diferentes estudos.

As revisões sistemáticas/metanálise têm origem na astronomia, passando pela agricultura, pedagogia, cujos métodos de síntese numérica de resultados foram desenvolvidos por estatísticos como R.A Fisher, L. Tippett, K. Pearson, E.S. Pearson, F. Yates, W.G. Cochran (2). Ainda que no início do século XX Karl Pe- arson tenha publicado uma síntese de resultados de estudos sobre a eficácia da vacina contra febre tifóide em soldados, a metanálise só ganhou expressão no campo médico a partir do estudo de Thomas Chalmers e Joseph Lau, sobre a eficácia da estreptoquinase para reduzir a mortalidade de pacientes com infarto agudo do miocárdio. Essa tendência ganhou fôlego com a criação, em 1992, da *Cochrane Centre* em Oxford, na Inglaterra, com o objetivo de preparar, manter e disseminar revisões sistemáticas de ensaios clínicos controlados.

**Etapas da revisão sistemática**

Qualquer revisão sistemática/metanálise deve ser precedida de um protocolo em que a estratégia a ser empregada deve ser especificada. As etapas de uma revisão sistemática/metanálise são apresentadas na figura 1. Perguntas claramente formuladas, juntamente com critérios claros de inclusão e exclusão de estudos, são imprescindíveis para o processo de identificação dos estudos pertinentes para a revisão/metanálise. É preciso ter clareza quanto às características da população para a qual se pretende responder a pergunta inicial, da exposição que se deseja investigar, assim como do desfecho que se quer mensurar. Cabe ainda definir quais os tipos de estudos que serão incluídos (ex: ensaios clínicos controlados, estudos caso-controle, estudos de coortes). Idealmente, uma revisão sistemática sobre procedimentos terapêuticos ou preventivos deve incluir apenas ensaios clínicos controlados.

Pergunta: Objetiva e operacionalizada de modo a ser testada.

Ex: A terapia hormonal melhora a osteopenia de mulheres na pós-menopausa?

Participantes: Caracterizar a população quanto ao sexo, faixa etária, características clínicas (quando for o caso). Por exemplo, mulheres no período pós-menopausa imediato, independentemente do estrato social, sem osteoporose. Definir o grau de osteoporose aceito na pesquisa.

Intervenção: Especificar qualquer hormônio ou um tipo específico.

Desfecho: Especificar como a melhora da osteopenia será definida, mensurada.

Tipo de estudo: Por exemplo, somente ensaios clínicos controlados.

Segue-se então a fase de identificação dos estudos perti- nentes. Restringir a busca ao *Medline* pode levar à ocorrência de distorções no resultado da revisão sistemática, dependendo do tema que se quer investigar. Há diversas bases de estudos para problemas específicos como o câncer, a atenção não-farmacológica aos doentes mentais, os transtornos de estresse pós-traumático, para citar alguns exemplos. Por outro lado, sabe-se que estudos com resultados negativos têm menos probabilidade de serem publicados, sobretudo nas grandes revistas indexadas, o que pode levar a um erro denominado viés de publicação. No caso de intervenções terapêuticas, o viés de publicação leva à detecção de eficácias inexistentes ou ao exagero na magnitude dessa eficácia.

Uma forma de minimizar o risco desse viés é expandir a busca para revistas não indexadas, anais de congressos, consulta a especialistas e pesquisa em *sites* de registro de ensaios clínicos, como aqueles presentes no endereço www.york.ac.uk/inst/crd/revs.htm.

Outro erro importante a ser evitado é a exclusão de artigos escritos em idiomas menos usuais. Sabe-se que estudos que mostraram resultados favoráveis às intervenções testadas cos- tumam ser

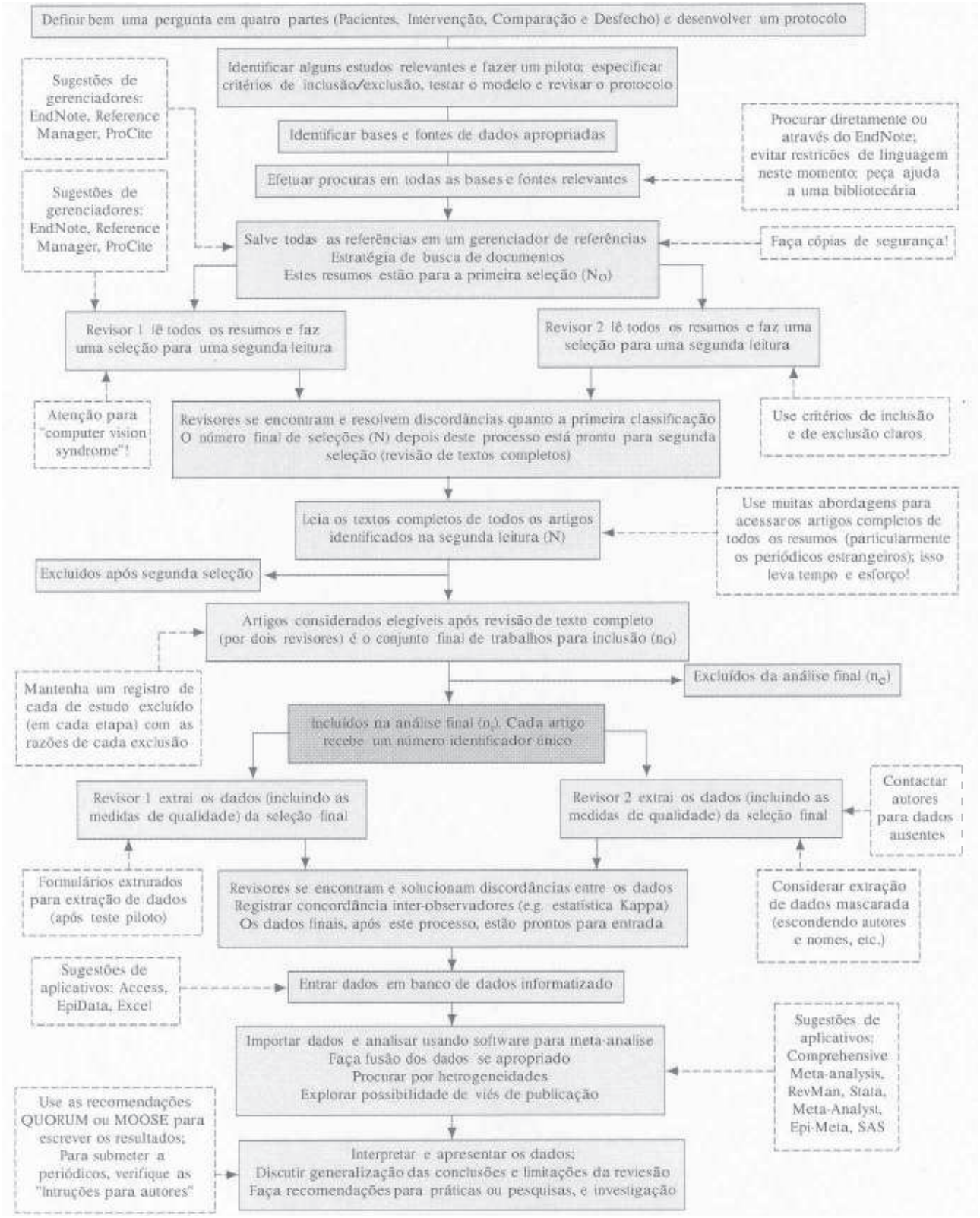


***Figura 1 -*** *Etapas de uma revisão sistemática.*
*Madhukar Pai, Michael McCulloch, Jack Colford. Systematic Reviews Group, UC Berkeley, 2002 [madhupai@uclink.berkeley.edu]*
*Traduzido para português por: Pedro Emmanuel A. A. do Brasil; Mestrando - IMS/UERJ, 2004 (pemmanuel@ig.com.br)*
*Disponível no site: http://www.medepi.net/meta/guidelines/Berkeley_Systematic_Reviews_Road_Map_V22_Versao_Brasileira.pdf*

publicados em inglês. Portanto, mesmo que não se possa traduzir artigos publicados, por exemplo, em alemão ou japonês, estes devem ser identificados na busca para que depois se avalie o possível impacto da sua exclusão sobre as conclusões da revisão.

Terminada a busca, o processo de seleção dos estudos começa com a avaliação dos títulos e resumos, quanto ao preenchimento dos critérios de inclusão. Nesta etapa, é importante, apesar de difícil, que os avaliadores sejam mascarados ("cegos") quanto à origem dos trabalhos. Desta forma, há chance de um trabalho ser incluído ou excluído apenas porque o avaliador já conhece o grupo ou porque o trabalho foi publicado em determinada revista. O uso de dois pesquisadores na leitura desses resumos pode reduzir o risco de não se detectarem artigos de interesse. A partir daí, devem ser obtidas cópias integrais dos trabalhos que estiverem de acordo com tais critérios ou sobre os quais exista dúvida sobre a pertinência para a revisão. É possível que estudos ainda sejam excluídos nessa etapa, devendo-se registrar o motivo dessa decisão. O processo de seleção deve ser documentado, preferencialmente num fluxograma. A Figura 2 apresenta o modelo proposto pelo "*Quality of Reporting of Meta-analyses* Group- QUOROM"3, com a documentação de quantos estudos foram excluídos em cada passo da seleção e o motivo desta exclusão. No caso de estudos observacionais, uma proposta de apresen- tação semelhante foi feita pelo "*Meta-analysis Of Observational Studies in Epidemiology Group–MOOSE"* 4.

Os estudos selecionados deverão ser avaliados quanto à qualidade metodológica, segundo critérios estabelecidos no pro- tocolo. Uma lista de 22 critérios usados para descrever a qualidade dos ensaios clínicos randomizados é descrita pelo *Consolidated Standards of Reporting Trials Grup-CONSORT*"5. Sugere-se que dois pesquisadores estejam envolvidos nessa fase, assim como na etapa posterior - a extração da informação.

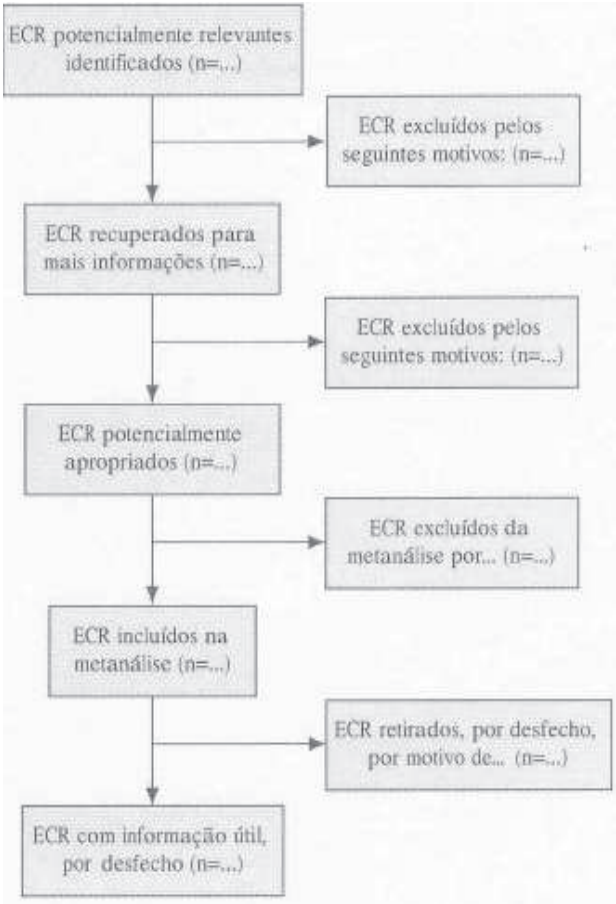


***Figura 2 -*** *Fluxograma com os estágios de uma metanálise de ensaios clínicos, proposto pelo QUOROM (3).*

## METANÁLISE: SÍNTESE QUANTITATIVA DOS RESULTADOS

### Medidas-sumário e *forest plot*

Se os estudos são homogêneos, pode-se combinar seus resultados para obter uma medida-sumário. Essa medida aumenta o poder estatísticoa e a precisão das estimativas, a partir do aumento do tamanho amostral alcançado com a combinação dos diversos estudos. No entanto, as técnicas estatísticas não são capazes de corrigir vieses no processo da revisão. Se a matéria-prima não é de boa qualidade, o resultado não é válido.

A medida-sumário é obtida a partir de uma média pondera- da dos resultados dos vários estudos, na qual os pesos são o inverso e suas variâncias. Em outras palavras, os estudos com mais precisão (maior tamanho amostral) recebem maior peso na estimativa combinada. Um dos métodos mais comumente usados para esse fim é o de Mantel-Haenszel.

Na Figura 3 construiu-se um gráfico (*forest plot*) com dados de uma metanálise conduzida por

[a] *Capacidade do teste estatístico em detectar um efeito da intervenção quando esta difere do grupo-controle.*

Roberts e Dalziel6 sobre a eficácia dos corticosteróides para acelerar a maturação pulmonar fetal em mulheres com risco de parto. Com pequenas variações, esses gráficos contêm os seguintes elementos:

a) Cada linha representa um estudo, sendo a estimativa do seu risco relativo (RR)b apresentada por um pequeno quadrado. A linha horizontal que corta o quadrado é o intervalo de confiança de 95%c. Observa-se que, em 13 dos 18 estudos, o intervalo de confiança inclui o valor nulo (risco relativo = 1), sendo esses estudos considerados inconclusivos.

b) O pequeno losango na parte inferior representa a medida-sumário. No caso da Figura 3, o risco relativo (RR) combinado foi de 0,69, o que significa redução (eficácia) de 31%d do risco de óbito neonatal no grupo cuja gestante fez uso de corticosteróide, na comparação com o grupo-controle. O intervalo de confiança de 95% desse RR (0,58-0,81, p<0,01) não inclui o valor nulo. Pode-se concluir que o uso pré-natal de corticosteróides em gestantes reduz o risco de parto prematuro em 31%, e que a probabilidade desse achado ser devido ao acaso é menor que 5%.

Os quadrados assinalando os RR de cada estudo apresentam tamanhos diferentes, sendo que o peso recebido pelos estudos na estimativa do RR combinado é proporcional à área do quadrado. O peso relativo de cada estudo aparece na coluna à direita do gráfico.

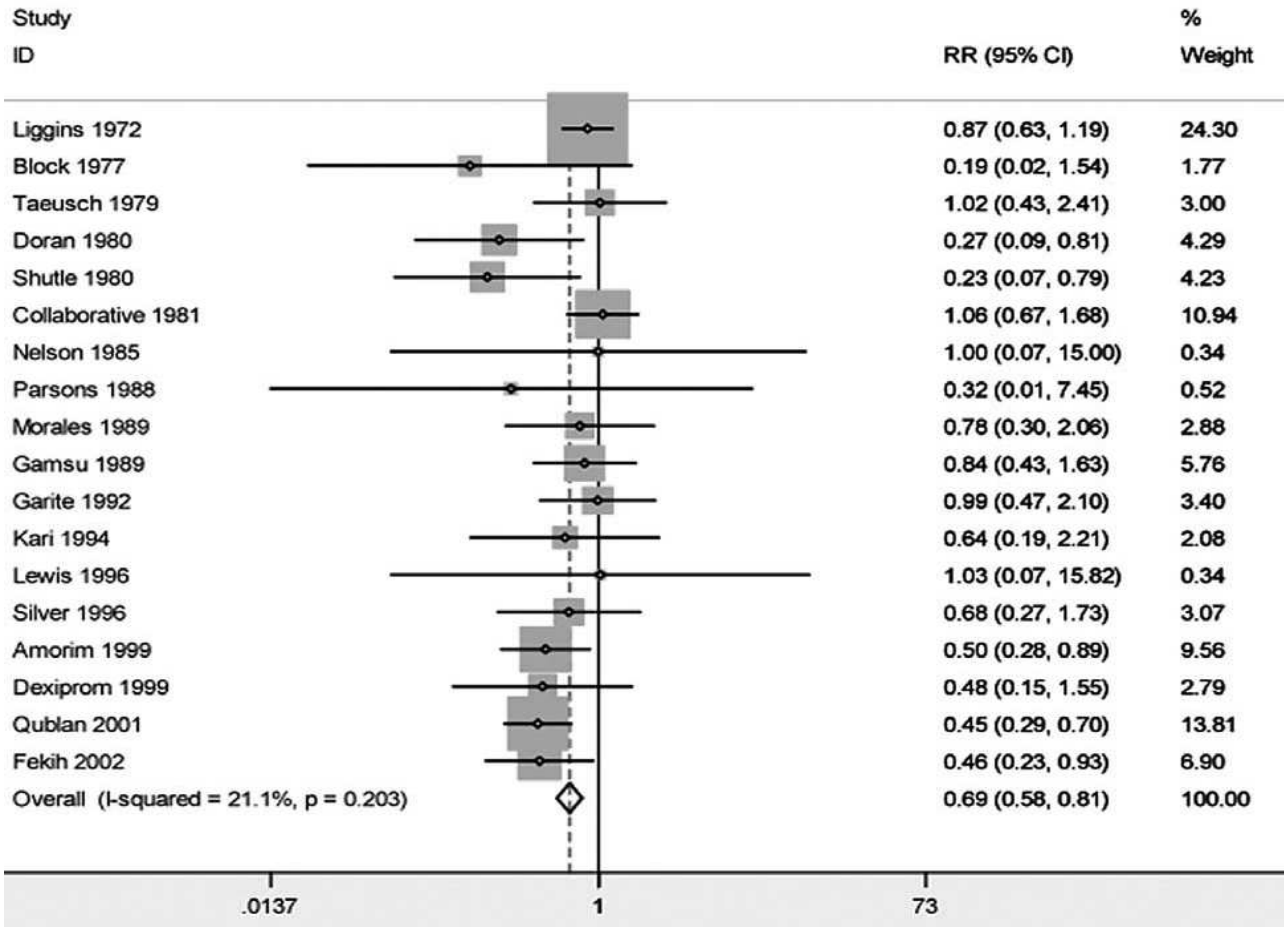


***Figura 3*** - Forest plot *com ensaios clínicos comparando os riscos relativos para óbito neonatal de prematuros em grávidas que fizeram uso de corticosteróides e de placebo. Gráfico produzido com o comando* metan *(efeitos fixos) do programa Stata 9.0, a partir de dados brutos apresentados em Roberts e Dalziel6.*

*[b] Risco de óbito neonatal no grupo de mães que receberam corticóide dividido pelo risco de óbito neonatal no grupo de mães que receberam placebo. O RR é igual a 1 quando não há diferença entre os dois grupos que estão sendo comparados.*

*[c] Faixa de valores que inclui, com 95% de confiança, o valor do RR caso todos os indivíduos, e não apenas uma amostra, tivessem sido estudados.*

*[d] Eficácia = (1-0,69) x 100.*

**Avaliando a heterogeneidade**

É comum que os estudos selecionados apresentem resultados inconsistentes. O fato de que a diferença entre eles supera o que seria esperado pelo acaso é definida como heterogeneidade estatística. Tal heterogeneidade reflete distinções entre os estudos, no que se refere a aspectos do desenho, que incluem diferenças na população estudada, na forma de mensuração da intervenção ou do desfecho, na qualidade metodológica dos estudos, entre outros4. Nesse caso, não faz sentido apenas ob- ter uma medida combinada, mas deve-se investigar os motivos desta inconsistência.

Thompson7 exemplifica esta situação com estudos sobre o efeito do uso de escleroterapia endoscópica de varizes esofagianas na redução da mortalidade de pacientes com cirrose hepática e da eficácia da redução do colesterol sérico na mortalidade por doença coronariana isquêmica. No caso da primeira metanálise, a heterogeneidade dos resultados pode ser atribuída às diferenças entre os estudos quanto à gravidade da doença de base (cirrose hepática), à técnica de endoscopia usada (intervenção), ao manejo das intercorrências e à duração do acompanhamento dos pacientes.

Duas estratégias para investigar os fatores ligados à heterogeneidade são: a análise de subgrupos e a meta-regressão. No caso da primeira, os estudos são subdivididos nos estratos da variável que se suspeita esteja causando a heterogeneidade. No caso da escleroterapia endoscópica, os estudos poderiam ser analisados separadamente, segundo a gravidade da doença de base, para formar grupos mais homogêneos. Esse procedimento demanda elevado número de pesquisas.

A meta-regressão é uma generalização da análise de subgrupos, que examina a relação entre os níveis de uma característica do estudo (ex: duração, dose, gravidade da doença, idade média do grupo) e a variação na medida de efeito (ex: risco relativo, diferença de risco, diferença de médias) dos trabalhos7. Sua implementação necessita que se faça uso de modelos multivariados, o que foge do escopo desse artigo.

## CONSIDERAÇÕES FINAIS

Embora a metanálise de ensaios clínicos tenha alcançado alto grau de aceitação na literatura clínica e estatística, alguns autores têm feito críticas sistemáticas ao seu uso em geral ou, mais especificamente, quando aplicada a estudos não-experimentais. A leitura desses artigos revela que grande parte das críticas está focalizada em aspectos metodológicos inerentes aos desenhos dos estudos sobre os quais a metanálise se constrói, sobre violações dos seus princípios metodológicos básicos ou sobre procedimentos metodológicos considerados inadequados em metanálise. Por exemplo, não é correto afirmar que a metanálise não considera a qualidade dos estudos ou a heterogeneidade entre os resultados deles, misturando "laranjas e maçãs". A qualidade é freqüentemente considerada tanto no processo de inclusão/exclusão de estudos quanto na avaliação dos seus possíveis impactos na conclusão.

Quanto à heterogeneidade, diversos artigos sobre metanálise têm chamado a atenção para a necessidade de se procurarem explicações para as inconsistências entre pesquisas e não se calcular medidas-sumário a partir da combinação de resultados heterogêneos. Para Liberati8, esse tipo de crítica decorrre de uma visão distorcida que considera a metanálise uma simples combinação estatística de dados.

Tudo o que foi dito anteriormente não isenta a metanálise de uma série de problemas. Pelo fato dela ser feita sempre depois que os dados já foram coletados, ela é suscetível aos vieses de pesquisa retrospectiva. É comum que metanálises sobre o mesmo tema encontrem resultados distintos.

Apesar das críticas, a metanálise tem sido considerada por muitos autores uma das mais importantes inovações na metodologia da pesquisa clínica. Movimentos mais recentes têm incorporado o conhecimento produzido pelas revisões sistemáticas/ metanálise. É o caso da medicina baseada em evidências e, mais recentemente, a saúde pública baseada em evidências. É neste contexto que Liberati8,9 lembra aos críticos desta metodologia que a única alternativa às revisões sistemáticas é efetuar revisões não-sistemáticas, cuja subjetividade e falta de critérios bem definidos são um terreno fértil para conclusões de pouca aplicação prática, ou mesmo erradas.

**ABSTRACT**

In the past decade, the Era of Evidence-Based Medicine, the number of meta-analysis dramatically increased. Meta-analyses statistically combine the results of multiple studies and are considered to be the highest level of evidence when the results of high-quality randomized trials are combined in an appropriate way. Results from a meta-analysis may not correspond to reality because of the large variation in the quality of the studies that have been pooled, and clinical and methodological differences among the included studies. The growing popularity of systematic reviews and meta-analyses has made it important to better understand them. The objective of this article is to help the reader comprehend how a systematic review and meta-analysis is carried out and to be better able to interpret them. We explain some impor tant aspects of conducting a meta-analysis. A better understanding of the basic terminology and the concepts involved in generating a systematic review and meta-analysis may help the clinician better evaluate the quality of a meta-analysis and the real importance of its findings for a specific patient.

**Key words:** Meta-analysis, Systematic Review, Clinical Trial.

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*Original Article*

# Laparoscopic Adrenalectomy – Analysis of 40 Cases of a Surgical Residency Service

## Adrenalectomia Laparoscópica: Análise de 40 Casos de um Centro de Residência em Cirurgia

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**ABSTRACT**

**Introduction:** Laparoscopic adrenalectomy in the past decade has become the method of choice for surgical approach to adrenal diseases. We analyzed a six year experience and the outcomes of 40 cases of laparoscopic adrenalectomy. **Objectives:** To analyze the safety, morbidity, and outcomes of 40 consecutive cases treated with transperitoneal laparoscopic adrenalectomy. **Patients and Methods:** We retrospectively analyzed 40 cases of laparoscopic adrenalectomy perfromed from January 2005 to October 2010, evaluating epidemiological factors, pathology findings, postoperative complications, and length of hospital stay. **Results:** The adrenalectomy was unilateral in all cases; 18 (45%) were right-sided; 22 (55%) were left-sided. 13 (32.5%) of the patients were men and 27 (67.5%) women. Anatomic pathology diagnoses were as follows: adenoma – 15, Cushing's syndrome – 3, pheochromocytoma - 4, Conn's Syndrome (aldosteronoma) – 3, metastatic lesions – 7 (Primary Tumors: lung-3, colon-1, prostate-2, breast-1), and others (angiomiolipoma -1, oncocitoma -1, Masson's tumor - 1, cyst - 2, aspergiloma - 1). The mean hospital stay was 2.1 ± 1.6 days and the mean operating time was 76 minutes. There was no conversion to conventional (open) surgery. **CONCLUSION:** The results of laparoscopic adrenalectomy were similar to those reported elsewhere and corroborate the safety and efficacy of the method resulting in an acceptable surgical time, faster postoperative recovery, and shorter hospital stay.

**Key words:** Adrenal tumor**,** laparoscopic adrenalectomy, complications, laparoscopy.

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## 1. INTRODUCTION

Laparoscopic adrenalectomy was first described by Gagner et al[1] in 1992 and quickly gained prominence as a safe and effective surgical therapeutic modality for the treatment of adrenal lesions. It is now considered the standard of care for most adrenal masses. Among the method's principal advantages are a shorter hospital stay, reduced intraoperative blood loss, and the less postoperative pain.[2]

The incidence of adrenal tumors varies from 1 to 7%, increasing with age.[3] Nowadays, the detection of most of these adrenal lesions occurs because of the widespread use of diagnostic methods ordered for other reasons. With early diagnosis, the disease course of functional adrenal tumors can be changed, permitting even cure in cases of early-stage adrenocortical carcinomas.[3,16]

## 2. PATIENTS AND METHODS

We conducted a retrospective analysis of the laparoscopic adrenalectomy cases performed by the General and Oncological Surgery Residency Service of the Santa Rita Hospital, in Maringá, Paraná between January 2005 and October 2010, with a mean follow-up 28 months.

The preoperative diagnosis of the lesion in the adrenal gland was made after an initial clinical suspicion or an incidental finding on ultrasound, and

was subsequently confirmed by computed tomography (CT), magnetic resonance imaging (MRI) when necessary, and biochemical assays (measurement of serum and urinary catecholamine levels, serum cortisol, renin and aldosterone). In two cases in which an aldosteronoma was resected, diagnosis was established by measuring renin and aldosterone collected by catheterization of adrenal veins. Laparoscopic surgery was contraindicated in patients who presented with lesions larger than 12 cm or that had malignant characteristics (rapid growth, calcification, and heterogeneity), signs of invasion of adjacent tissues, or vascular invasion.

The average age was 49.5 ± 16.1 years, with an average body mass index of 28.9 ± 4.7 kg/m$^2$. Among patients who underwent adrenelectomy,13 were men (32.5%) and 27 (67.5%) were women; 15% had previous abdominal surgery. All surgeries were unilateral, with 18 on the right (45%) and 22 (55%) left-sided.

The preoperative evaluation was carried out in conjunction with the endocrinology and cardiology group of the service; in all cases the functionality of the lesion was evaluated. In two cases of right-sided lesions in which there was a suspicion of emboli in the vena cava, magnetic resonance angiography was ordered. Both cases were negative for invasion or the presence of vascular emboli.

**Preparation of patients**

The clinical preparation of functional lesions took from three to eight weeks during which with time blood pressure and metabolic disorders were monitored. In cases suspicious for pheochromocytoma, the alpha-blocker prazosin is used, and the patient is hospitalized three days before the procedure for clinical management.

In the other cases, the patient was admitted on the eve of the procedure and asked to fast for eight hours. No bowel prep was performed. The patiient was shaved in the operating room. Antibiotic prophylaxis was a single dose of a first generation cephalosporin (Cefazolin). The surgical procedure was performed under general anesthesia with endotracheal intubation and passage of an orogastric tube.

**Surgical technique**

Once anesthetized, patients were placed in 90° lateral decubitus without the use of pads, stabilized in order to avoid injury to the neuromuscular bundles, with the return plate attached to the inferior leg.

The transperitoneal approach was chosen for all cases. Once patients were positioned, access was obtained using Hasson's (open) technique with the placement a 10mm trocar with camera in the subcostal position in hemi-clavicular line. Pneumoperitoneum was established by insufflation of carbon dioxide ($CO_2$) at a pressure of 12-14 mmHg.

Three additional five or 10 mm ports were then placed along the line of the rib cage (middle and posterior axillary line). A fourth port can be added, particularly in cases of right-sided adrenalectomies in order to displace the liver for proper exposure of the adrenal and inferior vena cava. After inspection of the cavity and adhesiolysis one proceeds with the mobilization of colic flexures as necessary.

On the right side after adequate exposure of the liver and release of ligaments, we chose the direct approach to the right edge of the vena cava with early identification and initial ligature with clips of the adrenal vein and accessory adrenal vein if present, followed by ligature of the middle adrenal artery.

Continuing with the detachment of the inferior portion of the adrenal gland separating Gerota's fascia from the upper pole of the kidney, ligating the inferior adrenal artery, and finally approaching the upper portion of the gland with ligature of the superior adrenal artery.

On the left side we begin with release of the freno-lienal ligament up to the diaphragmatic crus with dissection of the posterior aspect of the spleen and tail of the pancreas. Exposure of the spleen and pancreas medially exposes the renal vein and the main adrenal vein which is ligated between clips, followed by ligature of the branch of inferior phrenic vein. We opt for the initial ligature of the middle adrenal artery which is a direct branch of the aorta, followed by the superior adrenal artery (a branch of inferior phrenic). Finally with easier access to the pedicle, we performed the ligature of the inferior phrenic artery.

After complete release of the adhesions the surgical specimen is placed inside the extractor bag endoscopically, and then is removed after widening of one of the 10/12 mm ports. We close the muscle aponeurosis of the 10/12 mm trocars without a drain and the skin is closed with intra-dermal sutures.

All patients were evaluated every four months during the first three years and then semi-annually in the 4th and 5th years.

## 3. RESULTS

The forty adrenalectomies were unilateral. The histopathologic diagnoses of the lesions are presented in table 1. Most lesions were composed of adenomas (37.5%) and other benign lesions such as angiomyolipoma, oncocytoma, cyst and aspergilloma. Functional lesions were found in 25% of the cases. The principal metastatic lesions were prostate, lung, colon, and breast.

The mean length-of-stay and surgical time were 2.1 ± 1.6 days, and 76 minutes, respectively. Lesion ranged in size from 2.8 to 12 cm; the average size was 7.2 cm.

Intraoperative and postoperative complications included three cases requiring blood transfusion, including one due to a lesion of the splenic hilum; two cases of pneumonia and one wound infection; one case of pulmonary thromboembolism from deep vein thrombosis; and one case of a transient difficulty in dorsiflexion of the foot from compression of the right posterior tibial nerve (with recuperation in 5 months).

None of the cases that required transfusion needed to be converted to open surgery. There were no deaths from the procedure. Over the course of follow-up averaging 28 months, several patients with lung or breast metastases to the adrenal died from complications of their primary tumors, and one patient with hyperaldosteronism died of an acute myocardial infarction.

**Table 1 -** Histopathologic diagnosis of the adrenal lesion.

| Diagnoses | Cases |
|---|---|
| Adenoma | 15 |
| Adenoma (Cushing's Syndrome) | 3 |
| Pheochromocytoma | 4 |
| Aldosteronoma (Conn's Syndrome) | 3 |
| Angiomyolipoma | 1 |
| Oncocytoma | 1 |
| Masson's Tumor | 1 |
| Cyst | 2 |
| Aspergiloma | 1 |
| Ganglioneuroma | 2 |
| Metastatic* | 7 |
| **Total** | **40** |

**Primary Tumors: Lung: 3, Colon: 1, Prostate: 2, Breast: 1*

## 4. DISCUSSION

Since 1992, laparoscopic adrenalectomy (LA) has established itself as a safe and effective method for treatment of various lesions of the adrenal gland.[4] In 1996, just four years after the report of the first surgery, LA began to become the procedure of choice for the treatment of patients with small and benign adrenal lesions, due to its safety and efficacy, duplicating the outcomes of the conventional procedure. The training of surgical residents can be conducted in smaller centers, and when well run the results are similar to those of large series.

Adrenal tumors are classically divided into functional and nonfunctional, and benign or malignant. Most lesions are encountered/discovered as non-functional incidentalomas,[5,6] an experience replicated in our study. In a recent meta-analysis[6] 1800 cases of incidentalomas found from 1980 to 2008 were reviewed. Benign nonfunctional tumors accounted for 89.7% of the cases; in our series, however, the rates was lower (58%). Functional lesions such as subclinical Cushing's syndrome, pheochromocytoma and primary aldosteronism together represented about 10% of the cases. In our series about 25% of the lesions were functional, likely a consequence that our service receives referral from endocrinologists and cardiologists from various cities.

Only 2.6% of the lesions were malignant tumors: adrenocortical carcinoma 1.9% and metastasis 0.7%.[5,6] From the original series cases of carcinoma were excluded by preoperative imaging studies, thus 17.5% of our cases involved metastases to the adrenal referred by our oncology service.

The incidence of adrenocortical carcinoma (ACC) is approximately 1 case per 1,000,000 population with a bimodal age distribution with peaks at 5 and 50 years.[6,7] The clinical presentation of ACC was associated with Cushing's Syndrome in 45% of cases, and lower percentages of cases of virilization, feminization, or hyperaldosteronism.[8]

Although there is no consensus among the various authors, surgery for adrenal gland tumors is broadly accepted for the following indications: unilateral mass with documented pheochromocytoma and hyperaldosteronism, selected cases of subclinical Cushing's Syndrome, and adrenal masses with a suspicious appearance on imaging and/or a diameter exceeding 4 cm. [9,13,14]

With surgical conversion rates as low as 5%, low morbidity, earlier discharges and thus shorter hospitalizations, less postoperative pain, and better cosmetic results all contributed to the growing preference of the laparoscopic method.[9,10] Characteristics suggestive of malignancy found intraoperatively, adhesions, bleeding, and lesion size are the main reasons for conversion.

In our study there was no conversion, but the cases of longer operative time and splenic hilum injury occurred in patients with a BMI > 40. The single case of nerve damage occurred after loss of fixation of the patient during the table changes during surgery, which was only noted at the end of the procedure.

Among the intraoperative complications of the technique, the most common are vascular injuries, principally of the vena cava near the liver and of the left adrenal vein (0.7% to 5.4%), and intestinal, spleen, and pancreas injuries (1.3%).[9,10] All these complications can add significant morbidity to the procedure when not recognized quickly.[11] Various several serious and potentially fatal complications related to laparoscopic adrenalectomy have been reported, including: transection of the porta hepatis, ligature of the ureter, and loss of renal function secondary to ligature of the renal artery, which occurs more frequently in malignant lesions or in institutions beginning their experience. Prevention of such complications requires good knowledge of local anatomy, which includes a thorough preoperative investigation (which can include vascular studies of the adrenal gland) and which can determine a trans- or retroperitoneal approach; careful placement of the trocars under direct visualization and caution when manipulating the instruments outside the visual field of the surgeon.[12] Most injuries occur from the puncture with the Veres needle and from the placement of the first trocar, so we always chose the open technique with the first puncture.

The literature defines as determinants and limiting factors for the use of the LA method the size of the tumor and characteristics suggestive of malignancy. Parnaby et al[13] evaluated the role of laparoscopic surgery for tumors 6 cm or larger and came to the conclusion that as long as there was no local invasion, the results in terms of duration of anesthesia, postoperative complications, length of stay, and recurrence rates site were comparable to those obtained from surgical patients with tumors smaller than 6 cm. Currently, the contraindications to LA include the detection of invasion of peritumoral tissues in preoperative examinations and lesions with diameter exceeding 12 cm.[14] In our study we managed to extract a 12 cm ganglioneuroma, without complications, which after being bagged was extracted by a small Pfannenstiel incision.

Assessing malignant tumors, Miller published a retrospective analysis comparing laparoscopic and conventional techniques in the treatment of adrenocortical carcinoma. In this study, the average size of the lesions was 7.0 cm versus 12.3 cm (LA vs. Open) with recurrence occurring in 63% of the cases in the laparoscopic group and 65% of open group. The big difference was in the percentage with positive margins: 50% among those who underwent laparoscopic adrenalectomy (LA) and 18% for those who underwent open adrenalectomy. They concluded that considering that the only effective treatment recommended for adrenocortical carcinoma is surgical resection with free margins, LA should not be considered as initial treatment.

In all cases where an adrenocortical carcinoma was suspected our service opted for conventional surgery using the extended subcostal approach. There was one death in the immediate postoperative period due to release of a thrombus from the adrenal vein.

On the other hand, an Italian group evaluating LA for adrenocortical carcinomas found equivalence between the laparoscopic and conventional surgery for the disease in stages I and II when comparing recurrence rates, disease-free survival, and overall survival.[16]

Today, comparable results also have been obtained for laparoscopic resection of isolated adrenal metastases when evaluating by criteria such as margin involvement, local recurrence, disease-free interval, and mean five year survival. [17]

As part of the workup, computed tomography (CT) and magnetic resonance imaging (MRI) have great value in the differential diagnosis of these lesions, with CT the imaging study of choice for initial evaluation of adrenal masses. The evaluation of the enhancement of the images calculated in Hounsfield units during the CT scan allows one to distinguish benign from malignant lesions accurately. Among the invasive methods, fine needle aspiration (FNA) has low sensitivity for the detection of adrenocortical carcinoma, while somewhat better accuracy in the assessment of metastases to the adrenal gland.[18,19] Thus, due to its low sensitivity and the risk of seeding

tumor in the puncture path FNA is a little-used procedure in the diagnostic evaluation of adrenal masses.

Although well defined, in some situations, biochemical or radiological clinical tests do not always permit the preoperative identification of a malignant adrenal lesion requiring a conventional (open) surgical treatment.

With regard to the nature of the lesion to be addressed (benign, malignant, functional or nonfunctional) recent studies inform recommendations/guidelines for the various indications for LA. Thus, in spinal cord injuries and in cases of pheochromocytomas, in order to avoid the conversion, it is important to prepare the patient with alpha and beta blockers. In this way the conversion rate approaches rates of other functional lesions, thus avoiding an increased in the morbidity and mortality. [20]

## 5. CONCLUSIONS

Adrenalectomy is indicated for lesions exceeding 5 cm, lesions that are rapidly growing, when there is a suspicion of metastasis from other organs, and when the lesion is functional regardless of its size. In our series, laparoscopy was demonstrated as an effective method, with morbidity and mortality comparable to those of large series. Adrenocortical carcinomas in early stages with lesions less than 12 cm in diameter without signs of malignancy on CT appear to have outcomes equivalent to those obtained with conventional surgery. Thus, common sense should always guide the surgeon facing an adrenal lesion.

**RESUMO**

**Introdução**: A adrenalectomia videolaparoscópica desde o início da década de noventa vem sendo consagrada como método de escolha para abordagem cirúrgica das doenças da adrenal. Analisamos a experiência de seis anos e 40 casos. **Objetivos**: Analisar a segurança, a morbidade e os resultados de 40 pacientes submetidos à adrenalectomia videolaparoscópica. **Pacientes e métodos:** Análise retrospectiva de 40 casos de adrenalectomia transperitoneal laparoscópica realizados entre janeiro de 2005 a outubro de 2010, avaliando-se fatores epidemiológicos, achado anatomopatológico, complicações pós-operatórias e tempo de internamento. **Resultados:** Em todos os pacientes a cirurgia foi unilateral, sendo 18 à direita (45%) e 22 à esquerda (50%). Entre os 40 casos operados, 13 foram em homens e 27 em mulheres. Foram encontrados os seguintes diagnósticos anátomopatologicos: adenoma – 15 casos, síndrome de Cushing – 3, feocromocitoma – 4, aldosteronoma– 3, metastáticos – 7(pulmão-3, cólon -1, próstata-2, mama-1), ganglioneuroma – 2, e outras lesões benignas (angiomiolipoma- 1, oncocitoma- 1, tumor de Masson- 1, cisto -2, aspergiloma- 1). O tempo médio de internação foi de 2,3 ± 1,9 dias, o tempo médio de cirurgia foi de 76 minutos. Não houve casos de conversão para cirurgia aberta (convencional). **Conclusão:** Os resultados apresentados são similares aos relatados pela literatura, demonstrando que a adrenalectomia videolaparoscópica pode ser realizada de maneira segura e eficiente com benefícios como tempo cirúrgico aceitável e alta precoce.

**Descritores:** Tumor adrenal, adrenalectomia videolaparoscópica, complicações, laparoscopia.

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*Original Article*

# Dexamethasone for the Prevention of Postoperative Pain, Nausea, and Vomiting after Uncomplicated Laparoscopic Cholecystectomy. A Double-blind, Randomized Trial

## Uso de Dexametasona para a Prevenção de Dor, Náusea e Vômitos Pós-Operatórios após Colecistectomias Laparoscópicas Não-Complicadas. Um Estudo Duplo Cego e Randomizado

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**ABSTRACT**

The objective of this study was to investigate the effect of a single-dose of 8 mg of dexamethasone infused before induction of anesthesia to prevent pain, nausea, and vomiting after an uncomplicated laparoscopic cholecystectomy (LC). 70 non-consecutive patients who underwent uncomplicated LC were randomized to receive 8 mg of dexamethasone ($n$ = 37) or saline ($n$ = 33) intravenously 10-15 minutes before skin incision. Pain and nausea were measured on a visual analogue scale and the number of vomiting episodes after the surgery was registered. Dexamethasone did not change the perception of pain between the studied groups, but nausea sensation was relieved 1 hour ($p$=0.0004) and 6 hours ($p$<0.01) postoperatively. It diminished vomiting 1 hour after the reversion of anesthesia ($p$=0.0007), but this difference between the groups disappeared 6 and 24 hours after the reversion of anesthesia. In conclusion, 8 mg of intravenous dexamethasone decreased nausea and vomiting sensation after uncomplicated LC.

**Key words:** laparoscopy, glucocorticoids, anesthesia.

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## INTRODUCTION

Laparoscopic cholecystectomy (LC), a minimally invasive technique, is one of the most common elective surgical procedures in the western world. Compared to the conventional technique, it is associated with less surgical trauma and early return to activities of daily living.[1] Nevertheless, this technique is still associated with pain, nausea, and vomiting especially in the immediate postoperative setting, making the initial convalescence period unpleasant and uncomfortable.[2]

In the last few years, many drugs have been successfully used to prevent pain, nausea, and vomiting in the postoperative period.[2,3] Glucocorticoids have known analgesic and anti-emetic effects and are widely used by anaesthesiologists for these purposes, and yet the effectiveness of glucocorticoids is still questioned. There are studies which do not recognize the beneficial effects, and there are studies which demonstrate significant postoperative pain and nausea relief after preoperative dexamethasone infusion. Randomized clinical trials involving various major and minor surgical procedures have been conducted to examine the effects of preoperative administration of a single-dose of glucocorticoid on surgical outcome.[4] However, research protocols as well as the analyzed outcomes have been heterogeneous, which contributed to the inconsistency of the observed results. In particular, the general anesthesia protocols for pain[4,5] and nausea control are heterogeneous among the published observations. Because of this, the effectiveness of dexamethasone in the prevention of postoperative pain, nausea, and vomiting is unclear.

The purpose of this double-blind, placebo-controlled trial was to verify dexamethasone efficacy in the relief of pain, nausea, and vomiting in the first 24 hours after uncomplicated LC.

## PATIENTS AND METHODS

This was a prospective, randomized, double-blind placebo-controlled trial in which 8 mg of intravenous dexamethasone was administered to the treatment group and saline was administered to the control group 10-15 minutes before skin incision. The observed outcomes were essentially clinical parameters.

Between March 2009 and September 2010, 70 patients who underwent laparoscopic cholecystectomy were observed. The exclusion criteria were: physical classification III of the American Society of Anaesthesiology (ASA); younger than 18 years old or older than 75 years old; a body mass index > 30; pregnancy; signs of endocrine, renal, hepatic, immunologic or cardiac diseases; opioid or tranquillizer intake within one week of the procedure; treatment with steroids; a history of alcohol or drug abuse; a preoperative diagnosis of vesicular empyema, or previous endoscopic esphincterotomy for biliary ducts or stones; and motion sickness. Patients who presented transoperative complications such as conversion to laparotomy, acute cholecystitis, pneumoperitoneum time exceeding 90 minutes, scleroatrophic gallbladder, patients with intraoperative biliary duct lesions, and elevated blood pressure variations during the procedure were also excluded from the analysis.

All the patients were properly informed about the study and affirmed their voluntary participation by signing the informed consent document, written with the parameters recommended by the Ethics Committee of the University of Pernambuco.

The patients who agreed to participate in the trial were instructed about the research and about the symptoms measurement mechanism. Then, they were randomly divided into two groups by a computer program. Each patient was codified by a single researcher who was aware of the randomization assignment. This researcher prepared the drug and administered the drug intravenously to the patient 10 to 15 minutes before the skin incision. Anesthesiologists, patients, and surgeons were blinded to the procedure and had no knowledge whether dexamethasone had been administered or not. The researcher verified that the intra- and postoperative anesthesia and analgesia protocol was strictly obeyed, that the patient's demographic data were documented, and that the procedure was observed in order to ensure that the intraoperative exclusion criteria were followed.

The following drugs were administered to all the patients during general anesthesia: midazolam 5–15 mg, propofol 0.5–1.0 mg/kg, alfentanil 5-10 mg/kg, tracium 0.5 mg/kg, cefazoline 2 g, metoclopramide 10 mg, and inhaled sevoflurane. At the end of the procedure, prostigmine and atropine for neuromuscular paralysis reversion were administered. During anesthesia, the patient's cardiac rhythm and frequency, non-invasive blood pressure, pulse oxymetry, capnography, and intra-abdominal pressure were monitored.

A prophylactic and multimodal analgesic protocol was used for postoperative pain. Specifically, a total of 150 mg ropivacaine 0.75% was administered in all the trocar points before skin incision (50 mg in the 10-mm trocars and 25 mg in the 5-mm trocars), and ketoprofen (100 mg) was administered intravenously approximately 50 minutes before the end of the procedure. During the day of surgery, all the patients received dipirone 2 g intravenously every 8 hours. Additional ketoprofen was given when necessary. Additional doses of intravenous metoclopramide were administered for patients who presented with nausea with an intensity higher than 3 on the VAS.

The surgical approach consists in the establishment of a pneumoperitoneum which was created using an open technique. LC was performed using two 10 mm trocars and two 5 mm trocars, while maintaining a 12 mmHg intra-abdominal pressure. When necessary, an umbilical fascia incision was performed for gallbladder extraction. After the procedure, carbon dioxide was evacuated carefully from the abdomen. The nasogastric tube was removed from the patient before transfer to the ward. Throughout the 24-hour study, blood pressure, heart rate, and respiratory frequency were monitored every 6 hours, except during sleep.

After the surgery, a second researcher, absolutely blinded to the administered drug, assessed the patient's pain and nausea intensity according to the VAS presented to the patient before the surgery and registered the number of vomiting episodes (Figure 1). The data were stored using the patient's codification until the data analyses. The necessary information was obtained using standardized questionnaires, containing direct and easy to

comprehend questions that covered all the pre-established variables.

The pain and nausea grades and the number of postoperative vomiting episodes were quantified in the 1st, 6th, and 24th hours after the surgery. Pain and nausea were quantified using a VAS, and the associated pain and nausea intensity concepts (which range from absence of pain or nausea = 1, up to severe pain or nausea, non-responsive to medication = 5) as well as the number of postoperative emesis were computed. Pain was defined as a composite of incisional, visceral, and scapular pain. Nausea was defined as an imminent sensation of that one is about to vomit.

All the patients were discharged when their vital signs were stable and they could tolerate a light diet. Hospital stay was defined as the number of postoperative days (including the day of surgery) prior to discharge.

Data analyses. Data were expressed as mean values ± standard deviation, median ± range of distribution (min-max) or frequencies and percentages as appropriate. The Fisher exact test or ÷2, Student's *t* (two-tailed unpaired), and Mann–Whitney *U*-test were used to analyze proportions, as well as parametric and nonparametric data, respectively. Postoperative 24-hour results were specifically analyzed for intergroup differences. A $p < 0.05$ was considered statistically significant.

**Grade of Pain**

1 - Absence of pain
2 - Tolerable pain with moments when patient does not remember it or with low intensity. In both cases, there is no need for medication.
3 - Pain with moments when the patient does not remember it, but there is a need for analgesic drugs.
4 - Unforgettable pain, need for analgesic drugs control symptoms.
5 - Persistent pain, even with use of analgesic drugs; there is no significant improvement.

**Grade of Nausea**

1 - Absence of nausea
2 - Tolerable nausea, with moments when the patient does not remember or of low intensity. In both cases, there is no need for medication. Nausea ceased with one episode of vomit.
3 - Nausea, with moments that are forgotten. Need for analgesic drugs.
4 - An unforgettable nausea. Need for anti-emetic drugs to control symptoms.
5 - Persistent nausea, even with the use of anti-emetic drugs; there is no significant improvement.

## RESULTS

Thirty-three patients (47.2%) in the control group and 37 patients (52.8%) in the dexamethasone group were available for analysis. The groups were compared for age, gender, ASA score, skin color, and body mass index (BMI) (Table1). All the patients were discharged 24 hours after the procedure. There was no need to extend the hospital stay in any of the cases for any reason. Complications such as fever, surgical incision infection, coleperitoneum, and intraoperative bleeding were not diagnosed in any of the patients.

**Presence/absence of symptoms**

8 mg of dexamethasone was administered intravenously 10-15 min before the skin incision decreased the number of patients who reported any degree of nausea and vomiting at 1 and 6 hours after


***Figure 1** - A Visual analogue scale (VAS) used to measure pain and nausea.*

**Table 1 -** Comparison of patients' demographics between the dexamethasone and control groups. ASA score: American Society of Anesthesiologists' classification; BMI: Body Mass Index.

| | **Dexamethasone group (*n*=37)** | **Control group (*n*=33)** | ***P*** |
|---|---|---|---|
| Age (years) | 40.6 ± 2.2 | 41.9 ± 2.9 | NS |
| Gender (Female:Male) | 30:7 | 31:2 | NS |
| BMI | 27.4 (19.7-47.4) | 25.3 (19.1-46.5) | NS |
| Race (white/non-white) | 14/23 | 11/22 | NS |
| Married | 24/13 | 14/19 | NS |
| ASA score (1:2:3) | 25:12:0 | 24:8:0 | NS |

surgery. There were no differences between the two groups with regard to the number of patients who reported any degree of postoperative pain (Table 2).

## DISCUSSION

We demonstrated that when dexamethasone (8 mg) was administered intravenously 10-15 minutes before LC, postoperative nausea and vomiting were significantly reduced. No significant effects were observed in pain perception under the conditions of this clinical trial.

There are many reasons nausea and vomiting occurs after laparoscopic cholecystectomy: the use of anesthetic drugs, specifically opioids administered for the control of pain; the use of inhaled anesthetics; and the carbon dioxide utilized to induce and maintain the pneumoperitoneum. Dexamethasone has long been employed for the prevention of nausea and vomiting and for postoperative pain relief. The effectiveness of dexamethasone, however, is still a matter of debate because of the conflicting results from well-designed clinical trials.[5,6]

It is not possible, due to ethical reasons, to administer only intravenous dexamethasone for postoperative pain relief and nausea control or to fail to offer to the patient a safe and comfortable anesthesia in a clinical trial. For this reason, the clinical trials always include a safe anesthetic protocol and a postoperative protocol for pain and nausea management. This medical approach, which is ethically essential and justified, directly interferes with the perception of pain and nausea. As the trials employed different protocols that include drugs with

**Table 2 -** Number of patients who underwent LC who reported any degree of post-operative pain, nausea, or vomiting. Values in parentheses are percentages. Fisher exact test.

| | **Dexamethasone *n*=37 (52.9%)** | **Control *n*= 33 (47.2%)** | ***P*** |
|---|---|---|---|
| **Pain** | | | |
| 1 hour | 30 (81%) | 24 (72%) | NS |
| 6 hours | 26 (70%) | 26 (78%) | NS |
| 24 hours | 17 (45%) | 17 (51%) | NS |
| Nausea | | | |
| 1 hour | 6 (16%) | 20 (60%) | 0.0002 |
| 6 hours | 3 (8%) | 14 (42%) | 0.0016 |
| 24 hours | 2 (5%) | 7 (21%) | NS |
| **Vomits** | | | |
| 1 hour | 1 (2.7%) | 13 (39%) | 0.0001 |
| 6 hours | 1 (2.7%) | 9 (27%) | 0.004 |
| 24 hours | 1 (2.7%) | 4 (12%) | NS |

diverse mechanisms of action, as well as various routes of administration and dosages, it is not surprising that the results obtained were not entirely in agreement.[7,8,9,10] In the present work, we adopted a strict protocol for pain control that included opioids during surgery, local anesthetics at the points where trocars are introduced, and anti-inflammatory drugs. Postoperative opioid drugs were not prescribed so as not to increase nausea and vomiting. The adoption of this rigorous protocol for pain control may have hampered the recognition of the effect of dexamethasone in preventing postoperative pain. Under these clinical conditions, dexamethasone had no effect in preventing or decreasing postoperative pain, a finding this is consistent with the observations of others. Again, there are contradictory observations. Bisgaard and colleagues[5] employing a rigorous protocol for pain control that included fentanyl or alfentanil during general anesthesia, local anesthetic in all port sites, intravenous ketorolac, paracetamol administered using suppositories, and oral ibuprofen for pain control, and concluded that dexamethasone administered 90 min before LC reduced postoperative pain.

Prevention of nausea and vomiting following LC remains a medical challenge. Nausea and vomiting, regularly observed following LC, increase a patient's postoperative discomfort and suffering. The effectiveness of the powerful 5-HT3 receptor antagonist in the prevention of postoperative nausea and vomiting is disappointing.[11] Other antiemetic drugs such as droperidol have prohibitive side effects or, like metoclopramide, are relatively ineffective for the prevention of post LC nausea and vomiting.[3,12] Dexamethasone has been reported to reduce the incidence of postoperative nausea and vomiting and this effect is probably better than its effect in relieving postoperative pain.[13,14]

According to our observations, dexamethasone was effective for reducing the perception of nausea up to 6 hours after the surgery and for decreasing the episodes of vomiting up to 1 hour after surgery. These results are in accordance with others and are supported by systematic reviews about this matter. However, it is obvious that preoperative dexamethasone alone is not enough to prevent postoperative nausea and vomiting.

Some evidence suggests that the biological effects of dexamethasone begin 1-2 hours after administration. However, we and others administered 8 mg of dexamethasone 10-15 min before skin incision and observed results concerning prevention of nausea and vomiting similar to the ones published by Feo and colleagues and others who administered dexamethasone 90 min before surgery.[5] Presumably, the beneficial effects of dexamethasone in preventing postoperative nausea and vomiting are only realized when the patient has recovered from general anesthesia. Considering the time spent to induce general anesthesia, to securely operate the patient, and in recovering from the anesthesia, it is probable that dexamethasone had time to achieve a clinically acceptable effect. Thus we believe that it is not necessary to administer the dose of dexamethasone 90 minutes in advance, and we recommend the administration of 8 mg of dexamethasone a few minutes before the beginning of anesthesia.

In this work, we carefully applied criteria of exclusion. We included criteria for picking only healthy patients with uncomplicated gallstones subjected to straightforward and short (less one hour) LC. We concluded, under the conditions of this trial, that a single dose of 8 mg of dexamethasone administered 10-15 min before beginning LC can prevent and relieve postoperative nausea and vomiting. We believe that future trials should consider the most effective combinations of antiemetic drugs and their doses should provide an answer to the medical challenge of preventing and relieving postoperative nausea and vomiting.

**RESUMO**

O objetivo deste estudo foi investigar o efeito de uma dose simples de 8mg de dexametasona aplicada antes da indução anestésica para prevenir dor, náuseas e vômitos após uma colecistectomia laparoscópica (CL) não complicada. Setenta pacientes não-consecutivos que foram submetidos a uma colecistectomia laparoscópica não-complicada foram randomizados para receber 8mg de dexametasona (n=37) ou solução salina (n=33) intravenosa 10-15 minutos antes da incisão na pele. Dor e náusea foram mensurados numa escala análoga visual e o número de episódios de vômitos após a cirurgia foi registrado. A dexametasona não mudou a percepção da dor entre os grupos estudados. Houve alívio na sensação de náusea na primeira (p=0.0004) e sexta hora (p<0.01) pós-operatórias; além disso, episódios de vômitos diminuíram uma hora após a reversão da indução anestésica (p=0.00007) e as diferenças entre os grupos desapareceram 6 e 24 horas após a reversão da anestesia. Em conclusão, 8mg de dexametasona intravenosa diminuíram náusea e vômitos após CL não-complicadas.

**Palavras-chave:** laparoscopia, corticoids, anestesia.

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**Brazilian Journal of Videoendoscopic Surgery**

*Original Article*

# How do I treat Ovarian Dermoid Cyst by Laparoscopy?

## Como eu Trato Cisto Dermóide Ovariano por Laparoscopia?

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**ABSTRACT**

Laparoscopy is the gold standard for the management of benign ovarian cysts. Standardization of the surgical technique and the application of some tactics during the laparoscopic treatment of ovarian dermoid cysts increase the safety of the procedure and decrease the procedure-related morbidity. In this manuscript the authors describe the technical details of the laparoscopic management of ovarian dermoid cysts.

**Key words:** Benign cystic teratoma, dermoid cyst, laparoscopy, spillage.

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## INTRODUCTION

The dermoid cyst, also called benign cystic teratoma is a benign ovarian tumor common in women of reproductive age.[1] It corresponds to 20% to 25% of ovarian tumors and occurs bilaterally in 10 to 15% of cases.[2] Most dermoid cysts are asymptomatic and diagnosis is usually incidental during a routine pelvic exam or pelvic ultrasound.[3] The prevalence of malignant transformation has been reported in 1% to 3%.[2,4]

Surgical treatment aims to avoid potential complications such as torsion, spontaneous rupture (with subsequent chemical peritonitis), infection, malignancy, and possible loss of ovarian parenchyma due to progressive growth of lesion.[5] Traditionally, the treatment of dermoid cyst was ovarian cystectomy or oophorectomy by laparotomy, taking the utmost care to avoid contamination of the abdominal cavity with the intracystic content.[3] The main concern of the application of laparoscopy in the management of dermoid cyst is still the risk of leakage of intracystic contents into the abdominal cavity (spillage) in case of accidental rupture of the cyst, which can in theory produce a chemical peritonitis.[5-7] Although this risk appears to be low,[1] it should not be underestimated and some safety measures should be applied when dealing with dermoid cysts by laparoscopy.[5] In this article we describe the technical details of laparoscopic management of dermoid cysts.

## SURGICAL TECHNIQUE / PATIENT POSITIONING

The patient is placed in the lithotomy position, with arms alongside the body and thighs abducted, with a slight flexion. The bladder is catheterized with a 12 or 14 French Foley catheter.

## UTERINE CANNULATION

The uterine cannulation can be performed with a curette. The vaginal speculum is placed. The cervix is identified and the anterior lip, clamped with the aid of a Pozzi clamp. A curette is inserted through the cervix to the uterine fundus and secured to a Pozzi forceps with a sterile micropore. In this way, the uterus can be mobilized by the second assistant, facilitating surgical exposure of the pelvic organs.

## POSITIONING OF THE TROCARS/ PORTS

The Veres needle is positioned in the left hypochondrium point (Palmer's point), in the midclavicular line on the left, about 2 cm below the left costal margin.

The positioning of the trocars is standardized for almost all gynecologic laparoscopies, varying only in cases of large pelvic ovarian or uterine mass.

The 10mm trocar is positioned in the umbilical region and three 5mm trocars are positioned as follows: the first 2 cm medial to the left anterior superior iliac spine, the second in the midline, 8 to 10 cm below the umbilical puncture, and the third 2 cm medial to the right anterior superior iliac spine (Figure 1).

## APPROACHING/ADDRESSING THE DERMOID CYST

The importance of using an endobag to protect the pelvic cavity from the contents of the dermoid cyst in the event of its accidental rupture has been described in the literature.[5,8,9] The endobag is inserted into the abdomen through the 10mm umbilical port/ trocar and positioned below the ovary to be treated. From this moment, some technical variations can be applied to the procedure:

### Cystectomy without puncture

The ovarian parenchyma is coagulated in the contralateral portion of the pelvic infundibulum and sectioned superficially until one is able to identify the dermoid cyst wall. The sectioning is widened/extended to about 50% of the circumference of the ovarian parenchyma. Then the ovarian parenchyma is separated from the cyst wall using traction and countertraction. In some cases this separation can be achieved by means of grabbing each of the cut edges of the ovarian parenchyma and compressing them against the pelvic wall. In this way, the cyst is enucleated within the ovarian parenchyma. Usually some bleeding will occur is the proximity of the pelvic infundibulum, where bipolar coagulation is recommended before finalizing the freeing of the cyst from the ovarian parenchyma (Figure 2). The enucleated cyst is punctured inside the endobag and its contents are aspirated (Figure 3).

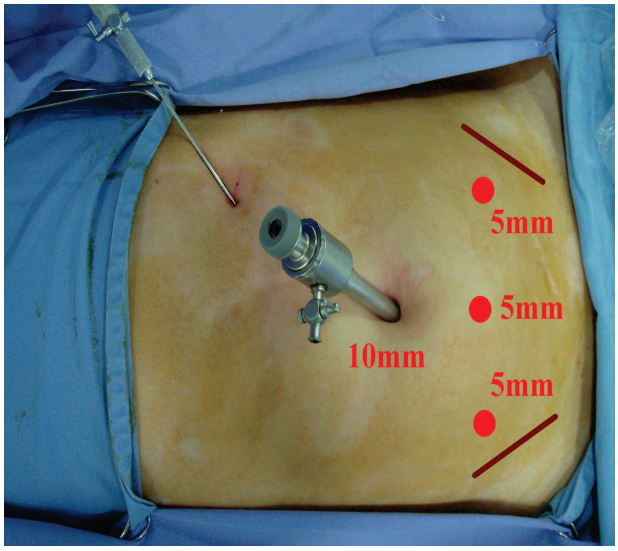


***Figure 1*** *- Classic Position of the trocars/ports in gynecologic laparoscopy.*

### Cystectomy after puncture

In this case, after the positioning of the endobag, the cyst is punctured using a laparoscopic needle and all its contents are aspirated. As it is predominantly sebaceous content and hair, aspiration is often not easy and occlusion of the suction system occurs. When opting for puncture before the cystectomy the ideal, then, is to have a 10 mm vacuum available.

Then, the cyst is irrigated and washed several times with 0.9% saline or Lactated Ringer's solution, taking care so that there is no leakage of the wash liquid. The separation of the cyst wall from the ovarian parenchyma is performed with the aid of three graspers, using traction and countertraction. (Figure 4)

### Oophorectomy

Normally oophorectomy is not the first therapeutic choice for women with ovarian dermoid cysts, since this disorder is usually identified in young women of reproductive age. We recommend oophorectomy only in those women during perimenopause.

The surgical technique is simple. After placing the endobag inside the abdominal cavity, the ovary is pulled by the assistant, who grasps the utero-ovarian ligament. The anterior layer of the broad ligament is coagulated and sectioned close to the round ligament, followed by coagulation and cutting of the posterior lamina of the broad ligament, toward/ in the direction of the pelvic infundibulum ligament. In this way, the broad ligament is fenestrated, leaving the ureter alongside the pelvic wall,

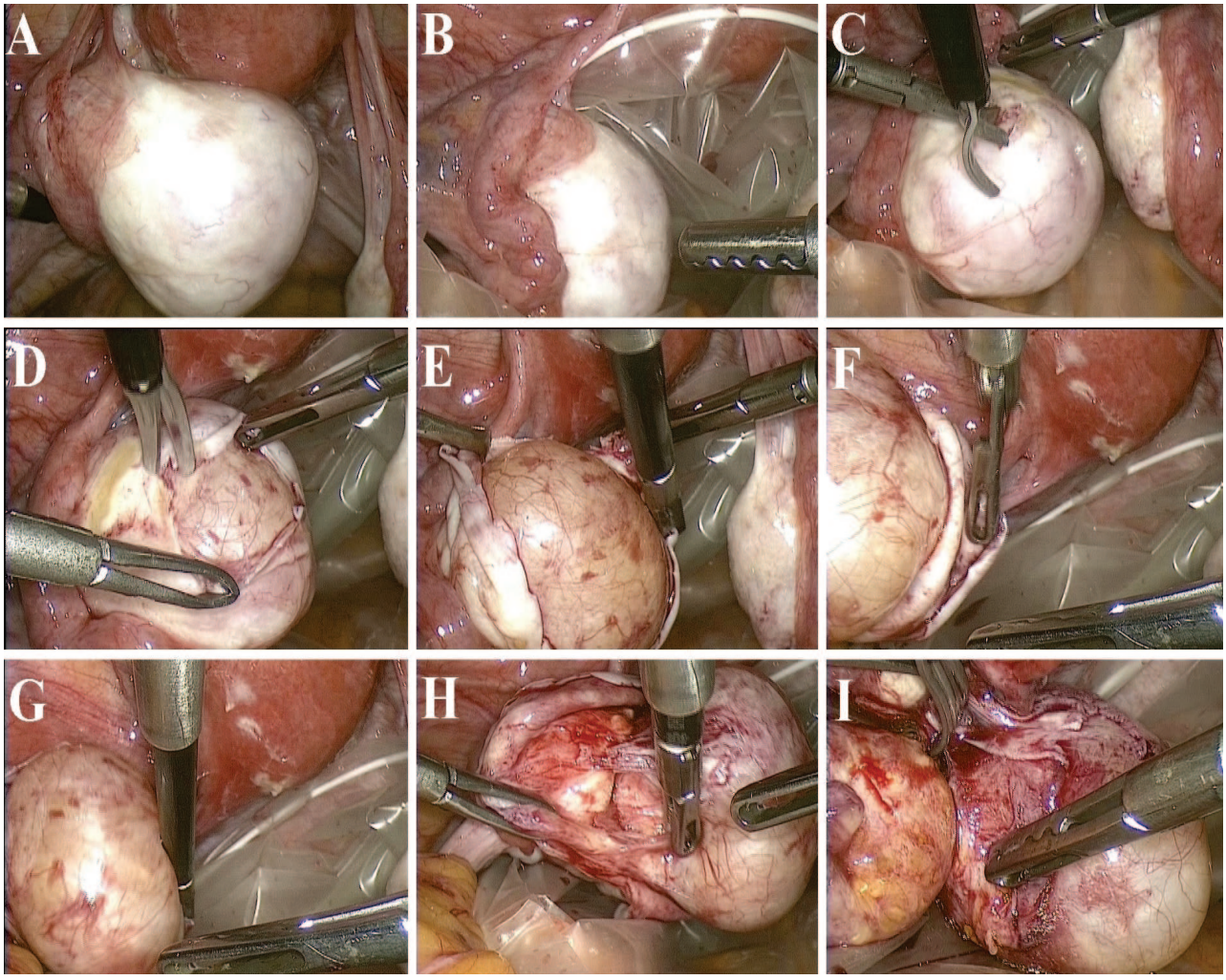


***Figure 2 -*** *(A) Dermoid cyst in left ovary. (B) Positioning of endobag under the ovarian lesion/cyst. (C) Opening of the ovarian parenchyma in the contra-lateral portion of pelvic infundibulum. (D) Enlargement of the opening in the ovarian parenchyma. (E to G) Enucleation of the dermoid cyst. (H and I) Finalizing the cystectomy.*

thereby avoiding iatrogenic ureteral injuries. The pelvic infundibulum is then coagulated and cut using bipolar forceps, harmonic bisturi/ scalpel, Enseal®, or linear cutting stapler. Finally, the utero-ovarian ligament is coagulated and sectioned. Another approach is, after fenestration of the broad ligament, perform the coagulation of the utero-ovarian ligament and fallopian tube, followed by the coagulation of the pelvic infundibulum (Figure 5).

The ovary is punctured inside the endobag and its contents are aspirated.

## WASHING THE PELVIC CAVITY AND REMOVAL OF THE ENDOBAG

The pelvic cavity is washed with 0.9% saline or Lactated Ringer's solution. In the event of accidental rupture of the cyst with contamination of

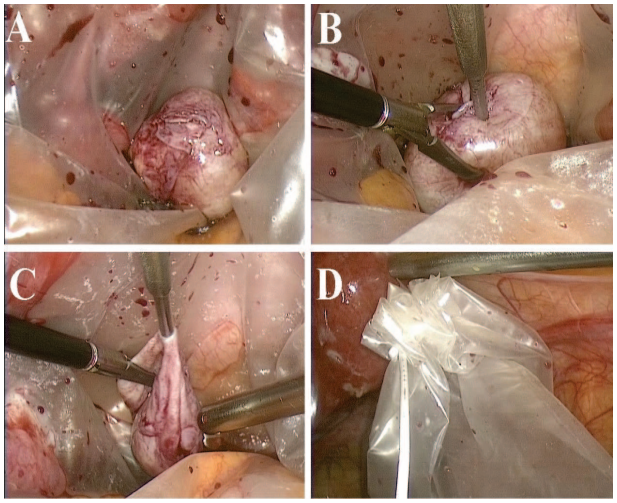


***Figure 3 -*** *Puncture of the dermoid cyst – enucleated from the ovarian parenchyma – using a laparoscopic needle, protected by the endobag.*

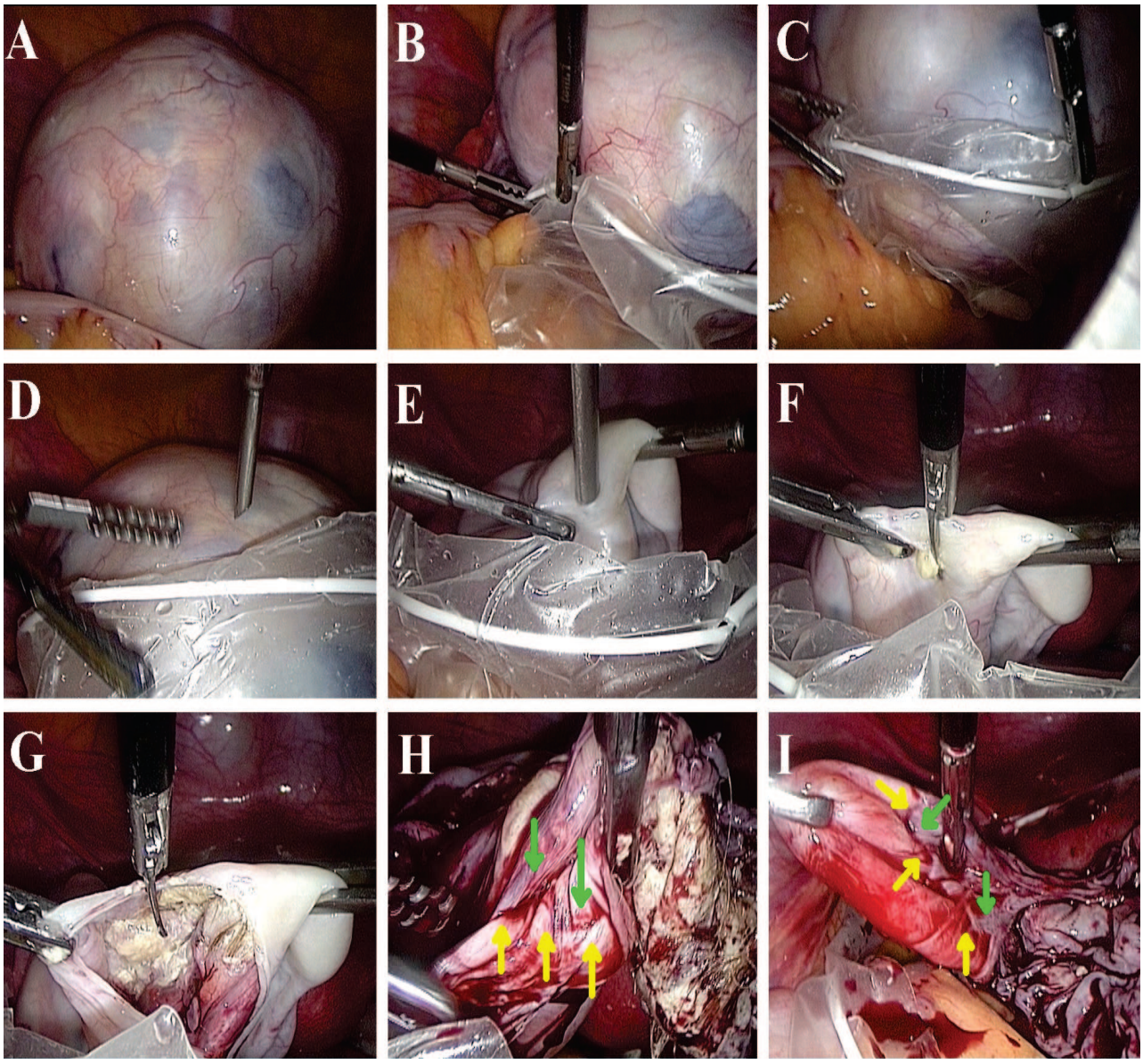


***Figure 4 -*** *(A) Dermoid cyst in left ovary. (B and C) Positioning/Placement of the cyst inside the endobag. (D and E) Puncture of the cyst with a laparoscopic needle. (F and G) Expansion of the orifice/puncture hole with scissors. (H and I) Separation of the cyst wall (green arrows) from the ovarian parenchyma (yellow arrows).*

the pelvis with intra-cystic content, copious washing of the pelvic cavity with about 4 liters of solution is recommended to prevent chemical peritonitis.[1]

Hemostasis is reviewed/revised with bipolar forceps/cautery. During this process it is prudent to support the outer surface of the ovary on the uterine wall and perform bipolar coagulation of the inner surface of the ovary (Figure 6).

The cyst is removed from the abdominal cavity inside of the endobag through the umbilical incision (Figure 7).

## CLOSING THE APONEUROSIS AND SUTURING THE SKIN

The aponeurosis of the 10mm umbilical puncture is sutured with zero vicryl, and the skin is sutured/closed with inverted sutures using 3-0 Monocryl.

## DISCUSSION

The treatment of benign ovarian cysts by laparoscopy is a reality. The benefits of laparoscopy

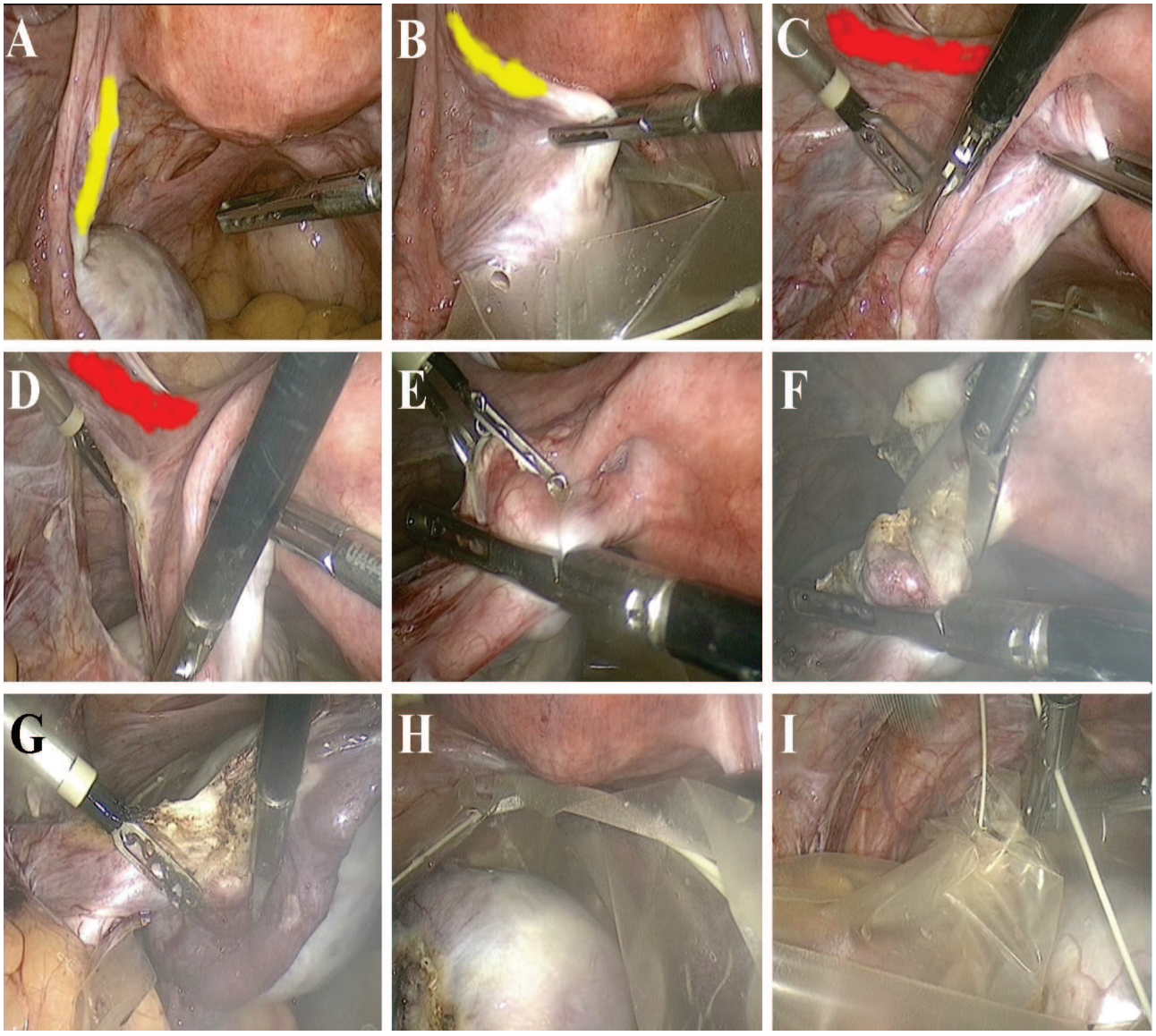


***Figure 5 -*** *(A and B) Mobilization of the left dermoid cyst through the manipulation of the utero-ovarian ligament (yellow). (C and D) Coagulation and cutting of the left broad ligament, fenestrating it from the round ligament (in red) to the pelvic infundibulum. (E and F) Coagulation and cutting of the utero-ovarian ligament and fallopian tube. (G) Coagulation of pelvic infundibulum. (H and I) Dermoid cyst within the endobag ready to be removed from the abdominal cavity.*

compared to laparotomy are well established in the literature: fewer postoperative complications (including fever and infection), less postoperative pain, shorter hospital stays, and lower total cost.[10] LIN and cols[11] compared cystectomy for dermoid tumors performed by laparoscopy and by laparotomy and found that laparoscopy was associated with a longer operative time, however, the hospital stay was shorter and the postoperative recovery faster. Similar findings were reported by BENEZRA and cols.,[12] who also identified a higher incidence of leakage of intra-cystic contents into the abdominal cavity with the laparoscopic technique (31.4% vs. 4.1%).

There is a common sense among gynecologic surgeons that extravasation of the contents of the dermoid cyst into the abdominal cavity can lead to complications (such as chemical peritonitis, the spread of infection or peritoneal irritation with subsequent formation of peritoneal adhesions) and this remains the biggest concern of laparoscopic treatment of dermoid cysts. Despite this increased risk of leakage when approaching/addressing the dermoid cyst by

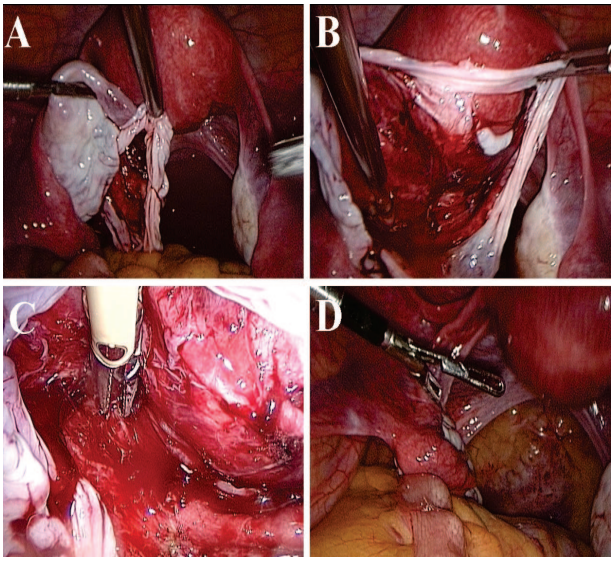


***Figure 6 -*** *Hemostasis of the ovary and revision/review of the abdominal cavity.*

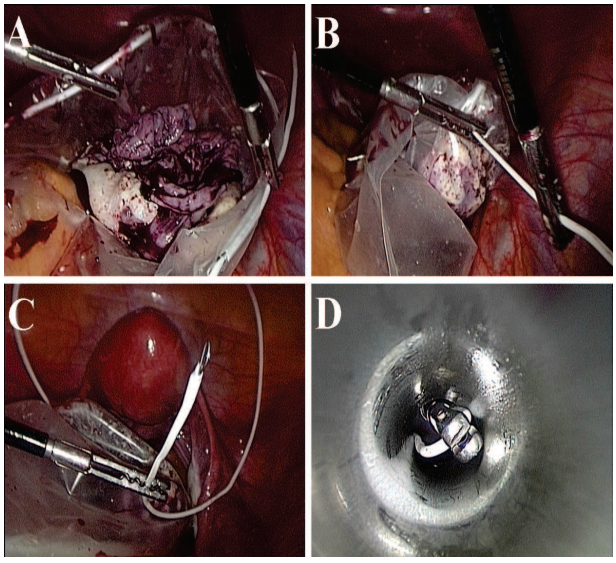


***Figure 7 -*** *(A and B) Positioning of the cyst inside the endobag and closing the endobag. (C and D) Externalization/Exteriorization of the endobag wire/string through the umbilical port/trocar.*

laparoscopy, most authors report that there is no increase in morbidade.[12, 13]

In the series of SHAWKI e cols.[1], the leakage occurred in 324 of 496 cases of laparoscopic cystectomy for dermoid tumor (65.3%), but chronic granulomatous peritonitis developed in only one of the 324 patients (0.3%). In the experience of the service of Clermont-Ferrand, the use of the endobag minimized or avoided/prevented contamination of the abdominal cavity in case of accidental rupture of dermoid cysts during laparoscopic cystectomy. The incidence of chemical peritonitis in this series was 8% (2 cases) when considering only the 26 patients in whom extravasation occurred and was not protected by an endobag.

In this article we present some important technical details to be followed during the laparoscopic approach of dermoid cysts. The use of endobag seems essential because it reduces peritoneal contamination in the event of accidental rupture of the cyst dermóide.[5, 8] In the event of extravasation, copious irrigation of the abdominal cavity with Lactated Ringer's solution or normal saline is indicated, in an attempt to remove even microscopic particles of the cyst content.[1, 9]

With advances in diagnostic methods, especially transvaginal ultrasound, dermoid cysts are being diagnosed while still small. The average diameter of these lesions when diagnosed is 50 to 70mm,[5,14] although they can be much larger. A lesion/cyst of this diameter is easily inserted into and manipulated inside the endobag. Puncture can be done at the beginning of surgery or after removal of the intact cyst. In deciding to perform the puncture at the start of surgery, one should be attentive to the need to irrigate the interior of the cyst in order to remove all of the intracystic content before proceeding to cystectomy.

When you choose not to perform the puncture at the beginning of the surgery one should perform movements delicately to avoid any accidental rupture of the cyst during the cystectomy. For lesions larger than 100mm in diameter, which do not fit inside the endobag, one option is to perform an open laparoscopy.[15] After the skin incision, the ovary is punctured and aspirated under direct vision through the umbilical incision. The puncture site is closed with a purse-string suture using 1vicryl and the ovary is reinserted into the abdomen. The laparoscopic cystectomy is then performed.

The preservation of ovarian function is feasible and effective for women of reproductive age suffering from benign ovarian cysts.[16] TSIKOURAS and cols.[17] observed an overall rate of intra-uterine pregnancy of 83.7% in a group of 43 women treated for ovarian dermoid cyst by laparoscopy, and who desired to become pregnant after surgery. One patient (2.32%) had an ectopic pregnancy.

Some authors[13] believe that the risk of recurrence of the dermoid cyst is greater when the treatment is performed laparoscopically, with a probability of recurrence within 2 years of 7.6% in

patients treated by laparoscopy and 0% in those treated by laparotomy. Probably the experience of the surgeon has a key role in the recurrence rate and the tendency is that, once the surgeon climbs/overcomes the laparoscopy learning curve, recurrence rates will be the same whether the dermoid cyst was treated by laparoscopy or laparotomy.

## FINAL CONSIDERATIONS

The benefits of minimally invasive surgery are unquestionable compared to open surgery. The standardization of surgical technique will ensure that the dermoid cysts are treated by laparoscopy safely and with minimal morbidity.

**RESUMO**

A laparoscopia é o padrão ouro para a abordagem de cistos ovarianos benignos. A padronização da técnica cirúrgica e a aplicação de algumas táticas durante o tratamento laparoscópico dos cistos dermóides aumentam a segurança do procedimento e reduzem a morbidade às pacientes. Neste artigo descrevemos os detalhes técnicos da abordagem laparoscópica dos cistos dermóides.

**Palavras chave:** Teratoma cístico benign, cisto dermóide, laparoscopia, extravasamento.

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**Brazilian Journal of Videoendoscopic Surgery**

*Original Article*

# Single Incision Laparoscopic Cholecystectomy: Description of a Series of 30 Cases of Laparoscopic Cholecystectomy Performed Using Conventional Instruments

## Colecistectomia Videolaparoscópica por Incisão Única: Série de 30 Casos Realizados com Instrumental Convencional

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**ABSTRACT**

**Introduction:** Laparoscopic cholecystectomy was considered a major milestone in the evolution of surgical technique at the end of 20th century and is today the standard for gallbladder surgery. Special equipment and materials have been developed to facilitate this practice. The development of minimally invasive techniques has reduced tissue trauma and improved cosmetic outcomes. Among them is Single Incision Laparoscopic Surgery (SILS), a new surgical approach that uses a single incision for laparoscopic surgery. **Methodology, patients, and surgical technique**: We report a series of 30 cases of laparoscopic cholecystectomy performed by the same surgeon, from April 2010 to February 2011, using common instruments and conventional laparoscopic surgical equipment via access through a single incision in the umbilicus scar. Following the usual laparoscopic surgical technique, the gallbladder was dissected visualization using 10 mm optics, with 0 and 30 degrees angulations. In twenty-one patients the bladder was pulled from its base with the aid of a surgical thread inserted through the abdominal wall. Twenty-five of the thirty cholecystectomies were performed in women; five in men. The patients' ages ranged from 21 to 66 years, with a mean 43.5 years. The duration of procedures ranged from 30 to 60 minutes with a mean of 45 min. No complications were recorded. The average hospital stay ranged from 6 to 18 hours; the average was 12 hours. There were no hospital readmissions. At the first outpatient follow-up visit, 3 to 7 days postoperatively, patient report rapid improvement of postoperative pain. **Conclusions**: In our initial series, we observed that SILS can be performed using conventional equipment and materials with proper safety, although uncomfortably. Thus, this procedure is a viable and promising approach that can be performed with conventional laparoscopic instruments; surgical comfort, however, could be improved with new tools and smart solutions to technical difficulties encountered.

**Key words:** Cholecystectomy, laparoscopic surgery, Single-site laparoscopic surgery, SILS.

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## INTRODUCTION

Since the end of the last century cholecystectomy performed by videolaparoscopy has been considered the gold standard technique for gallbladder removal due to its advantages over the open technique, including shorter surgical time, fewer complications related to surgical wound, fewer pulmonary complications, and faster return to work. Since then, surgeons have sought the development of less invasive techniques, reducing the number and size of the ports, thereby minimizing tissue trauma, further enhancing the aesthetic results, and ensure an even faster return to regular activities.

SILS (Single Incision Laparoscopic Surgery) is a new surgical approach that uses a single incision, preferably in the umbilicus for the performance of laparoscopic surgery. This new method has been used in a wide variety of laparoscopic surgeries, including tubal ligation,[5] hysterectomy,[6] appendectomy,[7,8] cholecystectomy,[9] gastrectomy,[10] colectomy,[11] and nephrectomy.[12] Several advantages have been observed with the use of a single incision, including the reduction of postoperative pain fewer complications involving tissue damage in the port site and scar lesions, with better cosmetic results. Special equipment and materials have been developed to facilitate the practice of this technique. In this series, we present 30 cases of SILS cholecystectomy using conventional laparoscopic materials.[13]

## METHODOLOGY, PATIENTS, AND SURGICAL TECHNIQUE

We report 30 videocholecystectomies performed by the same surgeon of the *Instituto de Mastologia e Clínicas Integradas* [IMAC] (Institute for Comprehensive Breast Care) between April 2010 and February 2011 in different hospitals, under general anesthesia, using common laparoscopic instruments and materials.

At the beginning of the procedure, the umbilicus was infiltrated with 10 ml of 1% Ropivacaine. Patients were positioned in dorsal decubitus, with the surgical team and the camera on the left, and the instrument nurse to the right of the patient. Pneumoperitoneum was established by Veres needle puncture and injection of carbon dioxide attaining a final pressure of 12 mmHg. (Figure 1)

Two 10 mm and one 5 mm diameter trocars were inserted in a single 15 to 20 mm "S" shaped incision in the umbilical scar. Under this single skin incision dissections of three areas in the subcutaneous tissue were performed through which trocars were placed seeking the formation of a triangle. (Figure 2)

Following the usual surgical technique the gallbladder was dissected and its hilum clipped, under

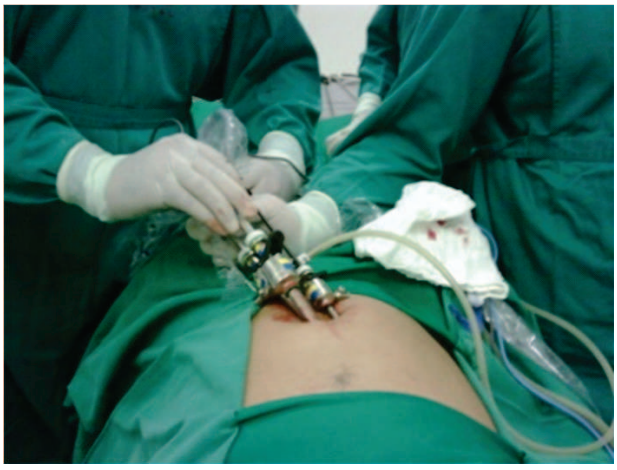

***Figure 1 -*** *Surgical positioning (surgeon of the left in the photos, assistant on the right).*

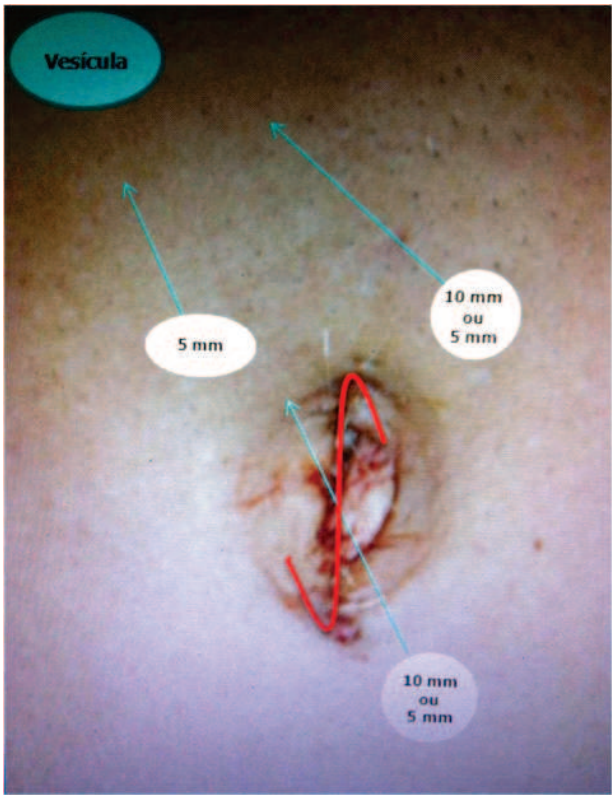


***Figure 2 -*** *Puncture locations (in torquoise) and location of the "S" shaped intra-umbilical incision (in red).*

visualization of 10 mm diameter optics with 0 and 30 degree angulations. In 21 of the patients the bladder was pulled from its base with the aid of a surgical wire inserted through the abdominal wall. (Figure 3)

## RESULTS

Twenty-five of the 30 cholecystectomies were performed in women, five in men. Patients' ages ranged from 21 to 66 years, with a mean of 43.5 years. The duration of the procedures ranged from 30 to 60 minutes with a mean of 45 minutes. No complications were recorded in intra- or post-operatively, except for 7 patients with bruising and maceration of the skin that resolved without repercussions or sequelae. The hospital stay ranged from 6 to 18 hours, with an average of 12 hours. There were no hospital readmissions. The first outpatient post-operative evaluation took place 3 to 7 days after discharge; all patients reported maximum pain on the Visual Analogue Scale (VAS) equal to 4 at that visit.

## DISCUSSION

Cholecystectomy is the most frequently performed laparoscopic procedure around the world.[14] This approach offers several advantages over the open technique, such as lower risk of wound infection, shorter hospital stay, faster return by the patient to their daily activities, and lower risk of incisional hernia.[15-17] These risks are even lower when a single incision is used, and thus, there has been increased interest in minimally invasive techniques for various surgical procedures, including SILS cholecystectomy.

In 1992 Pelosi et al described for the first time laparoscopic surgery with a single incision in a child requiring appendectomy.[18]In 1997 Navarra et al performed laparoscopic cholecystectomy with a single incision, using 2 transumbilical trocars and 3 transabdominal sutures passing through the base, neck and infundibulum of the gallbladder for better exposure of Calot's triangle.[19] Since then, many techniques have been described, but there is still no widely accepted standard.

The recent interest in SILS has led surgeons to use existing instruments to perform single-incision laparoscopy and has encouraged the industry to develop a variety of new instruments to facilitate these procedures. Several types of portals are already

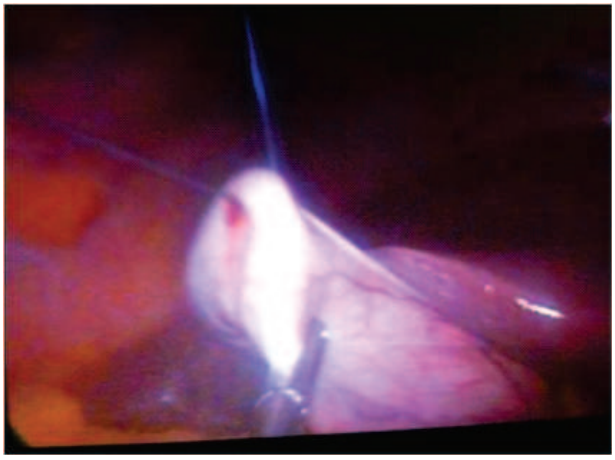

***Figure 3*** *- Suture pulling traction on the Bottom/base of the gall bladder.*

commercialized/sold, such as the TriPort (Advanced Surgical Concepts, Wicklow, Ireland), the SILS port (Covidien, Norwalk, Conn.), the Uni-X Single Port System (Pnavel Systems, Inc., Morganville, New Jersey ), the Anchorport (Surgiquest Inc., Orange, Connecticut) and Gelport (Applied Medical, Rancho Santa Margarita, California).[20] Still, we note that with proper training SILS can be performed with existing technology by surgeons experienced in conventional laparoscopy. And probably in the near future new instruments and materials will make this method increasingly utilized, with comfort and security extended to a larger number of surgeons.

The biggest challenge to overcome in SILS is to avoid conflict between instruments and the optic and reduce stress during surgery, due to the space constraints generated by a single incision, which requires more work of the surgeon and his assistant. For this reason, authors of several articles have proposed the use of the endoscopic camera and semi-flexible forceps, which can make the procedure more comfortable.[21] Several authors have also suggested percutaneous puncture of the gallbladder for drainage or for the introduction of suspension hooks for a better visualization of the triangle of Calot.[22-23]

Such maneuvers could increase the risk of gallbladder perforation with subsequent bile peritonitis, especially in the context of acute cholecystitis.[21] In addition, some difficulties may be encountered in accessing the abdominal cavity through a single incision in patients with a small umbilical ring, with an increased BMI, or adhesions from previous surgery. There are also technical difficulties due to the unavailability of a suitable portal, lack of instruments with angulation, short

length of the instruments, inadequate image quality, small incisions which make specimen extraction challenging, or leakage of pneumoperitoneum.[24]

The advantages of SILS cholecystectomy are related to a better aesthetic result, as it reduces the number of skin incisions to a single incision through a natural scar, the umbilical scar, leaving an almost invisible scar several months after the surgical procedure, and preserving body image. Moreover, it is believed that the SILS technique results in less postoperative pain, through the elimination of muscle damage and reduced tissue damage by virtue of the introduction of a single port, a lower risk of bleeding due to injury of the epigastric vessels,[25-27] and an earlier return to regular activities.

## CONCLUSION

We note that with the existing material and equipment, a team with advanced training in videolaparoscopy can perform videocholecystectomy through a single incision in reasonable time and with the proper safety. This procedure is feasible and promising, and can be performed with relatively less discomfort using conventional laparoscopic instruments. It will be important to conduct additional studies and develop new technologies that foster greater dissemination of the method, reduce the learning curve, and improve ergonomics affording increased comfort during surgery for the surgical team.

**RESUMO**

**Introdução:** A colecistectomia videolaparoscópica foi um marco na técnica cirúrgica no final do século passado, sendo hoje técnica padrão para remoção da vesícula. Têm-se buscado o desenvolvimento de técnicas minimamente invasivas e entre elas, a técnica denominada SILS (Single Incision Laparoscopic Surgery), a abordagem cirúrgica que utiliza uma única incisão, preferencialmente umbilical, para realizar a cirurgia videolaparoscópica. Diversos equipamentos e materiais especiais têm sido desenvolvidos para facilitar a prática desta técnica. Demonstramos nessa série, 30 cirurgias em que usamos material de videolaparoscopia convencional. **Metodologia:** Série de 30 casos de colecistectomias videolaparoscópicas realizadas por um mesmo cirurgião, entre abril de 2010 e fevereiro de 2011, utilizando material e equipamento comuns de videolaparoscopia e acesso cirúrgico por incisão única através da cicatriz umbilical. A técnica cirúrgica habitual foi seguida com dissecção da vesícula e clipagem de seu hilo, sob visão de ópticas de 10 mm de diâmetro e angulações de 0 e 30 graus. Em 21 destes pacientes a vesícula foi tracionada pelo seu fundo com auxílio de fio cirúrgico inserido através da parede abdominal. **Resultados**: A idade dos pacientes variou de 21 a 66 anos (média 43,5 anos). A duração média dos procedimentos foi de 45 minutos (variou de 30 a 60 minutos) e nenhuma complicação foi registrada no intra ou pós-operatório. O tempo médio de permanência hospitalar foi de 12 horas (variação de 6 a 18 horas) e todos os pacientes relataram dor máxima em E.V.A. (Escala Visual Analógica) igual a 4. Não ocorreram readmissões hospitalares. Na primeira reavaliação ambulatorial, entre 3 e 7 dias de pós-operatório, houve melhora significativamente rápida da dor pós-operatória. **Conclusão:** Observamos que com o material e equipamentos já existentes, uma equipe com treinamento avançado em Videolaparoscopia pode desempenhar em tempo adequado e com a devida segurança a videocolecistectomia por incisão única. Esse procedimento é viável e promissor e ainda que com relativo desconforto, pode ser realizado com instrumentos da videolaparoscopia convencional, sendo importante a realização de estudos adicionais e novas tecnologias para que haja maior difusão do método e maior ergonomia com aumento do conforto no ato operatório para a equipe cirúrgica.

**Descritores:** Videolaparoscopia, Colecistectomia, Incisão única, SILS.

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*Original Article*

# Videosurgery Learning and the Internet - How to Keep Yourself Up-To-Date Accessing the Virtual World

## O Aprendizado da Videocirurgia e a Internet – Como se Manter Atualizado Acessando o Mundo Virtual

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**ABSTRACT**

**Objective:** Present the main sources of research and medical-surgical teaching available on the worldwide web, facilitating the increasingly necessary academic upgrading of the surgeons. **Discussion:** The worldwide web is a resource with a growing presence. Medical sites, including those which focus on surgical education by providing classes, lectures, demonstrations of surgical techniques and others, are multiplying. The interaction between surgeons and the communication resources that information technology offers already make the availability of real-time communication with operating rooms a reality. **Conclusion:** The near future promises a broad and extremely beneficial relationship between these two areas of science, ever more interdependent, with a common goal: the benefit of our patients.

**Key words:** Surgical learning, internet, endoscopic surgery.

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## INTRODUCTION

The union of medicine with new technologies offers a new world of possibilities. Web-related services offered range from web sites specializing in the study and improvement of medical professionals to live transmissions of surgeries over the internet, video-courses, to the most sophisticated solutions such as remote surgical procedures.

The internet applications for surgical education are numerous and revolutionary. Cases can be discussed at a distance, videosurgeries can be tutored, and teaching workshops using virtual reality can be conducted with students in different countries and continents. All this is only possible because of the developments of the videosurgery era and the parallel development of high-speed Internet and optical components.

This review aims to present several present and future possible scenarios in which the teaching of videosurgery is linked with the Internet.

## MEDICAL EDUCATION PORTALS DEVOTED TO VIDEOSURGERY

In the area of education, Websites offer everything from search services specializing in the field of medicine (including surgery), such as Bibliomed, which is focused primarily on providing learning tools for students and health professionals, to specific guidance for the surgical specialties, like LapSurg and WebSurg, whose goal is to provide literature in support of online training in surgery.

Comprised of a team of collaborators from diverse fields, LapSurg Institute[1] is currently dived in two parts: the LapSurg portal and LapSurg Institute.

The LapSurg portal disseminates videosurgery knowledge and techniques. Video of surgeries, lectures, discussions are available. One of the distinguishing offerings of the portal are the surgeries broadcasted through the internet in real time. Accessing the site's restricted area you can consult

the collection, where you can find articles, lessons, surveys, interviews, and multimedia content.

Another portal accessed all over the world is WebSurg – the W*orld Electronic Book of Surgery*. It provides users with videos of surgery cases, tips, conferences, debates, interviews with experts, and specialized courses. The portal claims to offer the "largest collection of educational programs in minimally invasive surgery".[2]

Bibliomed provides leaning and training resources for the key medical specialties. It has offices in Brazil, Argentina and the United States, and its founders are large companies in the health sector, such as the Latin Healthcare Fund, and large medical groups as members of the host countries. The company offers two portals on the internet: Bibliomed and Good Health.

The Bibliomed portal provides scientific and educational presentations, applications for Palm PDAs, medical articles, images, news, diets, a Center of Toxicology, and Virtual Congresses. It has an area where subscribers can see full technical books and a section called "Professional Education", which contains links to medical periodicals, monographs and dissertations.[3]

Another portal, ABC Medicus, proposes that a well-informed patient, based on scientific information, can discuss with the doctor, extracting more concise informations from him and, in some ways, aiding in a quicker diagnosis. The user, when accessing the website, can watch videos, see photos, look for the meaning of scientific terms and symptoms in a specialized dictionary, and search for hospitals and doctor.[4]

Another option for videosurgery professionals is the *MedScape MedCenter*. This is an online platform owned by WebMD that offers professional content for physicians and other health professionals, in addition to offering education tools. The services offered range from review articles to views of professionals and various clinical cases.

Through the EBSCO *Information* Services portal called A to Z®[5,6], the subscriber can find articles, theses or monographs. The website has more than 81,000 essays submitted over 70 years from about 23 countries. When researching on the portal, you will get answers from some of the 17 most important medical databases available on the internet.

EBSCO DynaMed website for physicians has approximately 3,000 topics arranged in 36 categories. Dynamed differs from other portals; it does not offer direct search to technical articles or books and magazines, rather the website offers a search to summarized and reviewed material, as a medical encyclopedia.

The reader may feel confused when choosing among so many sources of information, so in Table 1 we present a comparison with the attributes that we consider most important in a medical portal. This table compares the main medical portals which provide material on videosurgery, according to the following features:

- **Dedication to specific issues:** considers if the website addresses specific topics in medical field.
- **Free Access:** considers if the website has areas where access is restricted to subscribers or has free access.
- **Articles, Theses, Books and Magazines:** considers if the portal has areas of research, reading, downloading or acquisition of technical work.
- **Interviews:** consider if the portal offers interviews with physician experts.
- **Multimedia:** indicates if the portal offers access or download of files of photos, videos or educational materials.
- **Forum:** considers the presence of a forum for discussion between doctors and patients or physicians.
- **Conferences, Courses and Congress:** informs if the website has an area for providing information on conferences, courses and congress or performs them online.
- **Glossary:** considers if the portal offers a glossary with detailed information about diseases or symptoms.
- **Debates:** considers if the website offers access to debates performe, doctors and researches, but without the interaction with the users.
- **Information for patients:** reports if the site has an area of information for patients or has language adapted for the lay public.

## SEARCH AND ESSAY PORTALS

Presented below are several sites that allow users to perform queries and provide access to the technical-scientific articles.

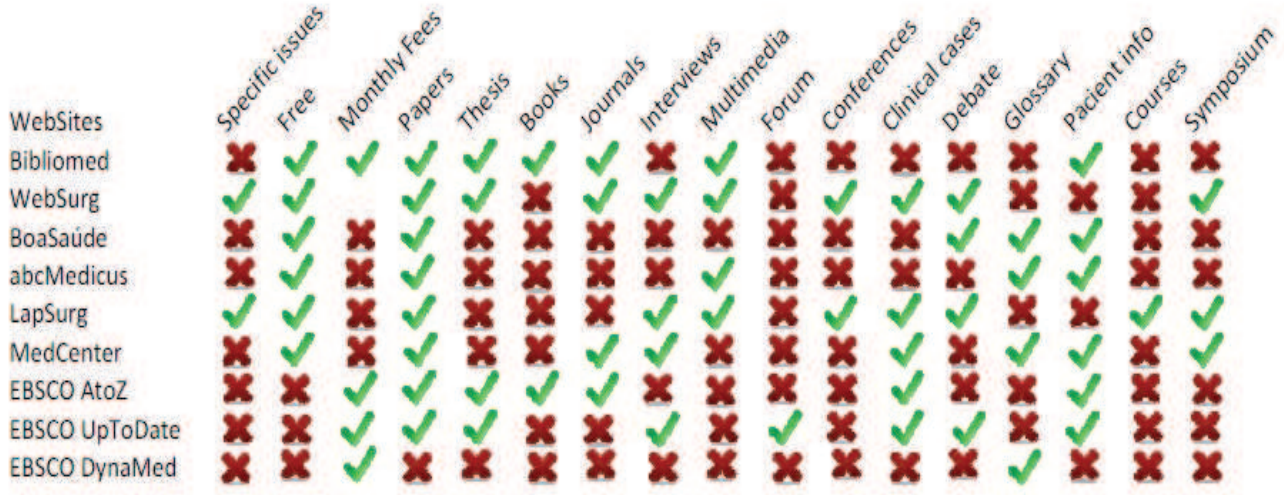


***Table 1*** *– Comparison among some medical-educationals portals.*

The Federal University of Sao Paulo (UNIFESP) offers the online library of the Department of Information Technology in Health, which allows the user to search for articles, books and journals. The library has 514 featured articles, 689 books, 2007 magazines (international), 116 Brazilian journals and 27 searchable databases.[7]

Elsevier provides the search tool *ScienceDirect*. Through this you can perform searches of articles or images that were or were not published in journals or books. The portal has a simplified structure that facilitates searches on databases and tools that streamline navigation such as: quick search, history of the links and navigation on homepage. *ScienceDirect* has an efficient search engine, returning to the user articles classified as published articles, accepted but unpublished articles, and as either free or available for purchase.[8,9]

Besides *ScienceSirect*, Elsevier also offers *Scirus*, which claims to be "the most comprehensive scientific research tool on the web" with more than 410 million articles indexed and 27 databases. The portal has a simple interface, very similar to that of Google[8,9].

The Virtual Health Library (*Biblioteca Virtual em Saúde* – BVS – in Portuguese) is the result of a partnership of the Ministry of Health, Ministry of Education, and Secretariat of Health of the State of São Paulo at Bireme – Specialized Center of the Pan American Health Organzation (PAHO). BVS offers a free tool to search information related to health area. The consortium involves Latin American, African and European countries and databases such as: BVS, *ePORTUGUESe*, GHL and *SciELO*.[10,11]

ProQuest® is a repository of electronic publications. It has a simple and intuitive interface, very similar to the *ScienceDirect*. In addition to searching to its own database, ProQuest conducts queries on the sites of other content providers. The user can conduct basic, advanced, topics and publications queries. The website provides another tool, Tesauro ProQuest®, which the user can enter subjects to search through a vocabulary list.

The American Society for Testing and Materials (ASTM), a century old society of engineers and scientists offers a search portal, the *Standards and Engineering Digital Library* (SEDL). The ASTM portal has a different focus from the websites described above. The website is focused on engineering; therefore, materials related to Bioengineering and Biomedicine are easily found.[13]

IngentaConnect™ is a service offered by *Publishing Technology*, which seeks to provide visibility for users publications by making their work available online, and offers a search engine of excellent quality. The website, which claims 25 million users, offers a database with over 13,000 publications from 25 publishers covering over 4 million articles. The portal offers free access; some results are classified as closed to free reading, requiring the purchase of the article.[14]

Proceed is a program of the Brazilian government, a partnership of the Ministry of Science and Technology and the Brazilian Institute of Information

in Science and Technology (IBICT), established in 1995 with the goal of promoting the use and creation of online information services. Proceed maintains collections of electronic documents on specific areas of knowledge. The user can select topics of interest to search, and can also access the Virtual Library of Notables of Science and Technology in Brazil where you will find biographies of important Brazilian scientists.[15]

The surgeon who wishes to obtain Brazilian scientific journals should visit the *SciELO – Scientific Electronic Library Online*. *SciELO* is an electronic library consisting of a collection of Brazilian scientific journals and created by the Foundation for the Support to Research of the State of São Paulo (FAPESP) – in partnership with BIREME and the Council for Scientific and Technological Development (CNPq).

*SciELO* users can access a wide range of journals, and view them issue by issue, with access to the complete text of articles. The journals and articles can be retrieved according to subject, author, an alphabetical list of journals, or by using the search tool.[16]

Aiming to distribute and promote the dissemination of books and journals for health professionals, the *Flying Publisher* company developed the websites www.*Freebooks4doctors.com* and www.*FreeMedicalJournals.com*. Both portals have the same interface and offer the same services, but are focused on the distribution of different content. The professional can navigate by topic, impact, or title of the material. If these options are not sufficient to find the desired material, the user may inform the topic, subject or title of work that is sought and perform that search through the search tool on the website.

*FreeMedicalJournals* has approximately 709 journals available, while the *FreeBooks4Doctors* website has about 365 books (Flying Publisher Books4Doctors, 2010).[17,18]

For professionals seeking to publish content online, CogPrints is a good tool. The portal, developed by the University of Southampton in England, offers this "auto archiving" service. The user, after registering, has the opportunity to include their works in the database of the website. The Cogprints portal classifies the published essays according to the year of publication and subjects addressed. Users can search by a piece of text, title, author or other information contained in the article.[19]

The *National Center for Biotechnology Information* (NCBI) offers users PubMed. PubMed is a search tool linked to the *U.S. National Library of Medicine* and the *National Institutes of Health*, with approximately 20 million biomedical citations from MedLine, books and journals online. The portal includes scientific articles encompassing the most diverse areas of medicine, including surgery.[20]

## CONCLUSIONS AND FINAL CONSIDERATIONS

The internet is transforming surgical education and the exchange of experiences in the field of videosurgery. The popularization of the high-bandwidth, high speed internet and easy-to-use applications on smartphones will accelerate this trend. In addition to the theoretical content available for study, videos and surgical animations are increasingly available on the worldwide web. Soon the resources of virtual reality and surgeries tutored at a distance will revolutionize surgical training and the way operations are performed around the world. This is especially true in regions of the globe where there are profound economic and scientific challenges for surgeons to maintain contact with advanced technology and keep up to date. Welcome to the future!

**RESUMO**

**Objetivo:** Apresentar as principais fontes de pesquisa e de ensino médico-cirúrgico disponíveis no mundo da web, tornando mais fácil a disponibilidade necessária para a atualização acadêmica dos cirurgiões. **Discussão:** O mundo da web é uma fonte com crescimento presente. Os sites médicos, incluindo aqueles com ensino em cirurgia que proporcionam aulas, cursos, demonstração de técnicas cirúrgicas dentre outras, estão se multiplicando. A interação entre cirurgiões e fontes de comunicação, as quais são oferecidas pelas informações tecnológicas, torna uma realidade possível à comunicação em tempo real com os centros cirúrgicos. **Conclusão:** O futuro próximo promete uma relação ampla e extremamente benéfica entre estas duas áreas científicas, cada vez mais interdependentes, com um objetivo em comum: o benefício de nossos pacientes.

**Palavras chave:** Aprendizado cirúrgico, Internet, cirurgia endoscópica.

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*Review Article*

# Thymectomy by Video-Assisted Thoracic Surgery in Myasthenia Gravis

## Timectomia por Cirurgia Torácica Vídeo-Assistida na Miastenia Gravis

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**ABSTRACT**

Laparoscopic surgery provides a minimally invasive alternative to open resection of the thymus in the control of Myasthenia Gravis. It is easy to see the increasing number of publications from groups of surgeons who are adopting this technique, bringing valuable information from their results. This article presents a summary of the different techniques of video-assisted thymectomy with their results and also describes the technique used by the authors of the work and case series.

**Key words:** Video-assisted thoracic surgery, thoracic surgery, *myasthenia gravis*, thymectomy.

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## INTRODUCTION

The Myasthenia Gravis (MG) is an autoimmune disease resulting from changes in the neuromuscular junction, characterized clinically by abnormal and prolonged fatigability of striated muscles that is worsened by repetitive action or tension and regain strength with rest or with the use of cholinesterase inhibitors. Its relationship with the thymus is evident and current treatment of its generalized form includes thymectomy.

Videosurgery has brought us a new option with the possibility of performing a more radical resection with a less invasive technique and, that consequently causes less morbidity and mortality.

## MYASTHENIA GRAVIS

The treatment is performed with the use of anticholinesterase drugs, corticosteroids, immuno-suppressants, plasmapheresis or immunoglobulin and/or by removing the thymus.

There is considerable controversy regarding the best treatment for the control of Myasthenia Gravis. Spontaneous remission occurs naturally, but unpredictably. Results after thymectomy are highly variable; some patients experience complete remission while others no improvement whatsoever. For some the post-thymectomy response occurs only after several years. And yet, there seems to be a consensus for surgical therapy, as this presents remission rates or rates of clinical improvement that are significantly higher than in the groups treated only with medications. [1,2,3,4,5]

There are different types of surgical access, such as transcervical, partial or total transsternal, combined cervical-sternal, or resection by video-assisted thoracic surgery (VATS). The Myasthenia Gravis Foundation of America (MGFA) classified the various forms of thymectomy which are performed in myasthenic patients and gives a percentage of thymic and perithymic tissue that each technique can remove.[6]

- T-1 Transcervical Thymectomy
  a. Basic (40% to50%)
  b. Extended (75% to 80%)
- T-2 Videoscopic Thymectomy
  a. Classic VATS (80% to 85%)
  b. VATET
- T-3 Trans-sternal Thymectomy
  a. Standard (70%to80%)
  b. Extended (85% to 95%)
- T-4 Transsternal and Transcervical Thymectomy (98% to 100%)

The MGFA also published a modified clinical classification of Myasthenia Gravis.[6] (Figure 1)

In adults with generalized disease, thymectomy is always indicated, once the diagnosis is established. This early indication for surgery seeks a more rapid and complete remission, or at least an increased chance of improvement. [2,3,5,7,8,9] Others only recommend surgery in cases in which clinical control has failed.[10,11] In the pure ocular form, many agree that when clinically controlled, surgery is not necessary,[10,12,13] except when they present evidence of generalized disease demonstrated by electromyography and not evident clinically, or when a thymoma is present.[5,14,15]

| | |
|---|---|
| Class I | Any ocular muscle weakness<br>May have weakness of eye closure<br>All other muscle strength is normal |
| Class II | Mild weakness affecting other than ocular muscles<br>May also have ocular muscle weakness of any severity |
| IIa | Predominantly affecting limb, axial muscles, or both<br>May also have lesser involvement of oropharyngeal muscles |
| IIb | Predominantly affecting oropharyngeal, respiratory muscles, or both<br>May also have lesser or equal involvement of limb, axial muscles, or both |
| Class III | Moderate weakness affecting other than ocular muscles<br>May also have ocular muscle weakness of any severity |
| IIIa | Predominantly affecting limb, axial muscles, or both<br>May also have lesser involvement of oropharyngeal muscles |
| IIIb | Predominantly affecting oropharyngeal, respiratory muscles, or both<br>May also have lesser or equal involvement of limb, axial muscles, or both |
| Class IV | Severe weakness affecting other than ocular muscles<br>May also have ocular muscle weakness of any severity |
| IVa | Predominantly affecting limb and/or axial muscles<br>May also have lesser involvement of oropharyngeal muscles |
| IVb | Predominantly affecting oropharyngeal, respiratory muscles, or both<br>May also have lesser or equal involvement of limb, axial muscles, or both |
| Class V | Defined by intubation, with or without mechanical ventilation, except when employed during routine postoperative management. The use of a feeding tube without intubation places the patient in class IVb. |

***Figure 1***

The cases best suited for resection include the generalized form of myasthenia that required progressive increases in medications for control of symptoms, or those that present a poor response to these medications with myasthenic crises and/or repetitive cholinergic crises, and those that do not experience a spontaneous remission after a long course of medication.[16]

The only situation in which, no doubt, all agree with the formal indication for surgery in Myasthenia Gravis, is when we see the presence of a thymoma. To prevent recurrence the resection should be as complete as possible, removing the entire thymus gland – a procedure called "thymothymomectomy" – and when necessary, resecting nearby invaded structures *em bloc* (lung, pleura, pericardium, great vessels) along with tumor implants and nodules when present (radical or extensive surgery).[17,18] The preferred path for this surgery is sternotomy, but there are reports of resection via a suprasternal approach[19] and even video-assisted thoracic surgery for those thymomas in stage I.[20,21,22] On the other hand, the main factors that are associated with longer survival were the presence of complete encapsulation, removing the entire tumor, small size and predominance of non-epithelial cell in the tumors, with 10 year survival ranging from 78% to 95% in Trastek and Payne stages I and II.[23]

The **MGFA** proposed a standardization of the assessment of the myasthenic state after thymectomy, defining every type of patient response quite well. [6] (Figure 2)

## CHANGE IN STATUS

Improved (I) - A substantial decrease in pretreatment clinical manifestations or a sustained substantial reduction in MG medications as defined in the protocol. In prospective studies, this should be defined as a specific decrease in QMG score.

Unchanged (U) - No substantial change in pretreatment clinical manifestations or reduction in MG medications as defined in the protocol. In prospective studies, this should be defined in terms of a maximum change in QMG score.

Worse (W) - A substantial increase in pretreatment clinical manifestations or a substantial increase in
MG medications as defined in the protocol. In prospective studies, this should be defined as a specific increase in QMG score.

Exacerbation (E) - Patients who have fulfilled criteria of CSR, PR, or MM but subsequently developed clinical findings greater than permitted by these criteria.

Died of MG (D of MG) - Patients who died of MG, of complications of MG therapy, or within 30 days after thymectomy.

## THYMECTOMY BY VIDEO-ASSISTED THORACIC SURGERY

Landreneau in 1992 published the first report of a thymectomy performed using videosurgery in the treatment of a patient with myasthenia gravis and a thymoma. [24]

Currently, there are a large number of surgeons performing thymectomy in myasthenic patients by video-assisted thoracic surgery, with removal only of the gland, without any concern for carrying out the removal of the pericardial fat and the perithymic tissue.[20,22,25,26,27]

Videothoracoscopy can be performed with access through the left hemithorax: with the patient in a supine position and the left side elevated approximately 30º to 45º, three to four incisions are made anteriorly between the midaxillary line and internal mammary artery.[29,36] Kaiser et al operated on 15 patients through the left hemithorax using this technique. Nine thymomas were encapsulated. A complementary left inframammary minithoracotomy was performed frequently. [25]

Those who use a complementary anterior cervical incision, with or without a sternal elevator, report that it is easier to free the superior poles and ligate the thymic veins.[28,29,30,31]

Those who perform thymectomy on the right side position the patient in left lateral decubitus, placing three to four incisions – for the introduction of instruments in right hemithorax – between the anterior axillary line and the scapula. They report that they can free the superior poles up to the neck without cervicotomy. [25,26,32,33,34,35,36]

Mack and Scruggs (1998) demonstrated the performance of type T2a thymectomy with the extension described and documented their technique with photos. Many who perform the type T2a thymectomy, however, performed a more limited resection according to the assessment by Jaretzki. [35]

According to Yim and cols. the use of this technique was associated with a reduced need for analgesics in the postoperative period ($p < 0.05$), a shorter hospitalization (five days on average) ($p < 0.05$) and an increase in operative time (107.8 + / -22.2

| | |
|---|---|
| Complete Stable Remission (CSR) | The patient has had no symptoms or signs of MG for at least 1 year and has received no therapy for MG during that time. There is no weakness of any muscle on careful examination by someone skilled in the evaluation of neuromuscular disease. Isolated weakness of eyelid closure is accepted. |
| Pharmacologic Remission (PR) | The same criteria as for CSR except that the patient continues to take some form of therapy for MG. Patients taking cholinesterase inhibitors are excluded from this category because their use suggests the presence of weakness. |
| Minimal Manifestations (MM) | The patient has no symptoms of functional limitations from MG but has some weakness on examination of some muscles. This class recognizes that some patients who otherwise meet the definition of CSR or PR do have weakness that is only detectable by careful examination. |
| MM-0 | The patient has received no MG treatment for at least 1 year. |
| MM-1 | The patient continues to receive some form of immunosuppression but no cholinesterase inhibitors or other symptomatic therapy. |
| MM-2 | The patient has received only low-dose cholinesterase inhibitors (< 120 mg pyridostigmine/day) for at least 1 year. |
| MM-3 | The patient has received cholinesterase inhibitors or other symptomatic therapy and some form of immunosuppression during the past year. |

***Figure 2***

minutes) ($p < 0.05$) compared to thymectomy by sternotomy. They performed eight thymectomies in myasthenic patients by video-assisted thoracic surgery, with two thymomas in stage I. [33] Savcenko and cols. (2002) in 10 years of experience performed 47 T2a thymectomies in myasthenic patients by direct right videothoracoscopy. They had a 2% conversion rate (for bleeding) and had an average hospital stay of 1.64 days. With an average follow-up of 53 months the change in status according to the MSFA parameters was a CSR of 14%, PR of 8%, MM of 39%, I of 22% , U of 14%, and W of 3%. [58]

Locertales and cols. (2004) performed 25 type T2a thymectomies from the right side with no mortality and with three conversions (two for bleeding and one because of difficulty with the surgery). The mean hospital stay was 4.2 days. The cohort were followed for periods ranging from 14 to 68 months. Eleven patients were asymptomatic without medication, 10 patients were improved with medication, and four patients had no improvement in their myasthenic condition. This author reported that after surgery two patients were found on computed tomography imaging to have thymic remnants in the left hemothorax; both underwent a new left-sided videothoracoscopy.[36]

Ruckert and cols. (2000) in an anatomic and surgical study of cadavers demonstrated that resection was more incomplete when the surgical access was from the right rather than from the left.[37]

Chang and cols. (2005) conducted a prospective study comparing 15 patients who underwent thymectomy by bilateral videothoracoscopy and 16 patients who underwent post-sternotomy thymectomy (type T3b thymectomy). Their significant findings were that the video-assisted technique had a longer operative time, but less intraoperative bleeding. The two groups had a similar frequency of remission of myasthenia, but the patients who underwent type T3b thymectomy – as measured using a visual pain scale – had significantly greater pain complaints during the first three months post-operatively.[38]

The first report of the performance of an "extended" thymectomy with videothoracoscopic resection of the entire thymus and bilateral pericardial fat associated with a cervical exploration using a sternal elevator – known as as Video-Assisted Thoracoscopic Extended Thymectomy (VATET) or resection type T2b – was published by Novelino and cols. (1994). They reported performing 10 thymectomies in myasthenic patients, including two stage I thymomas, using a transverse cervical incision and bilateral videothoracoscopy with trocars entering the 1st intercostal space in anterior axillary line and two along the lateral inframammary line in the 2nd and 5th intercostal spaced, initially performed on the left, with the patient in a supine position.

The operative time ranged from 50 to 300 minutes; the mean hospital stay was five days.[28] Scelsi and cols. (1996), Saito and cols. (1998) and Mantegazza and cols (2003) also performed this same technique of extended thymectomy.[29,31,39]

Mantegazza and cols. (2003) compared 157 myasthenic patients who underwent VATET with 47 myasthenic patients who underwent extended transsternal thymectomy (type T3b resection) and concluded that the frequency of complete remission (Kaplan-Meyer curve) was similar, and thus is a valid alternative to T3b surgery in MG, with low morbidity, and better acceptance of the cosmetic result.[29]

In 2004 Bramis and cols. published a report of 10 patients who underwent Video-Assisted Transcervical Thymectomy (VATT). With a mean follow-up of 63.8 months there was 90% improvement rate.[40]

Another form of extended thymectomy by thoracoscopy in myasthenic patients was described by Zielinski et al who used a neck incision and a subxifoide incision, introducing the sternal elevator through these two incisions. The optic was introduced first through the right hemithorax and then through the left hemithorax. These authors reported that in 100 patients operated, 71% had ectopic thymic tissue, mainly in perithymic tissue (37%) and in the aortic-pulmonary window (33%). Of these, 48 patients were accompanied for one year; 83% improved while there was one death from Myasthenia Gravis. Twenty five patients were accompanied for two years; 32% had complete remission.[41]

The resection of thymomas in stage I, and of thymic cysts using thoracoscopy was also performed by other surgeons.[26,42]

The effectiveness of this type of surgery is still unknown due to lack of follow-up time, but some report a response similar to that obtained with other thymectomy techniques.[26,29,34,35] As it is still a novel operation performed in few patients to date, there are advances in the instrumentation and surgical technique that are ongoing. With regard to the selection of patients, there is a tendency to recommend surgery in cases of Myasthenia Gravis of recent onset and milder

symptoms and in younger patients.[22] Those who perform video-assisted thymectomy report the advantages of performing a complete resection of the gland, with less pain, less morbidity, shorter hospital stays, and better cosmetic results.[20,25,26,33] These same advantages were also found in several other procedures performed by thoracoscopy.[43,44,45]

As this technique requires appropriate and expensive equipment, and training of the surgeon, it really has a higher initial cost, but this is offset with a shorter hospital stay, with lower morbidity, and a faster return to work.[20,25]

Because it is still a new technique, there are disadvantages such as a substantial increase in time under anesthesia with bronchial blockade, operating using a flat screen with only two-dimensional vision, and the loss of the sense of palpation.[46]

Special attention was given by some surgeons to the issue of trauma to the intercostal neurovascular bundle from the trocars with the onset of acute or chronic pain.[11,47] Landreneau and col. found no significant difference in the onset of chronic pain in patients undergoing pulmonary resection by thoracotomy or video-assisted thoracic surgery. [47]

In order to reduce the trauma of the intercostal nerves some surgeons advocate a partial resection of the rib[11] and the others do not use trocars, threading entry of instruments directly through the incision.[48] This can be achieved by flexion of the operating table in order to increase the intercostal spaces of the patient in lateral decubitus position, avoiding the exaggerated inclination of the thoracoscope during the procedure.[33]

It has been clearly observed that as more operations are performed, there is a decrease in operative time.[49] With the presence of a magnification camera, there is a better view of the tissue to be dissected with excellent illumination and the additional advantage of being able to demonstrate the procedure to assistants and students, and record all the steps of the operation on video.[49]

Certainly there is a promising future for videothoracoscopy with the technologic advances improving the optics, the staplers, and the instruments in general.

With advances in robotic surgery, some centers have performed thymectomy reporting advantages due to the precison in the dissection due to the three dimensional image and the instruments developed with much greater mobility when compared with those of video-assisted surgery. [50,51]

## OUR SERIES

Our study cohort is composed of 48 patients with Myasthenia Gravis who underwent thymectomy by video-assisted thoracic surgery from May 1995 to February 2011. Of these, 42 were by the extended technique with cervical access and right and left videothoracoscopy, with type T2b (VATET) resection. In four patients thymectomy was performed by right-sided videothoracoscopy, and in two the thymectomy was performed by right neck incision and right-sided videothoracoscopy (Figure 3) .

Of the 42 patients who underwent extended thymectomy, 37 (88.0%) were women and five (12.0%) were men; their ages ranged from 17 to 70 years. Two patients had thymomas, both about 3 cm in size. The classification of the myasthenia gravis of these patients was based on MGFA. (Table 1)

As preoperative preparation, all patients – except for patients in Classes IIa and IIIa – underwent two to three sessions plasmapheresis (with an interval of 24 hours between them), the last plasmapheresis

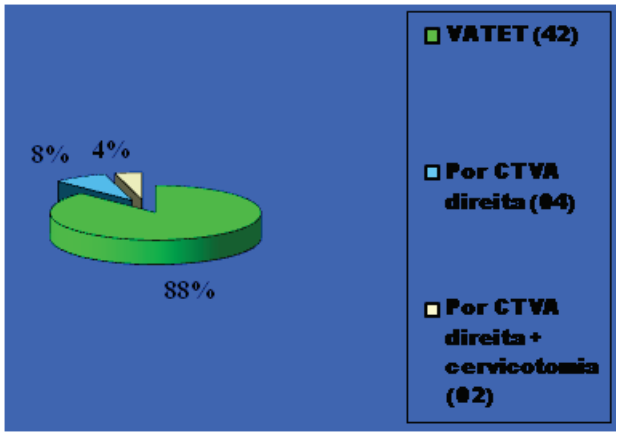


***Figure 3*** *- Gráfico das cirurgias realizadas.*

**Table 1**

| | # of Patients | |
|---|---|---|
| Female | 37 | (88.0%) |
| Male | 5 | (12.0%) |
| Age | 17-70 | years |
| IIIb | 38 | (91.2%) |
| IIIa | 2 | (4.8%) |
| IIa | 1 | (2.4%) |
| IVb | 1 | (2.4%) |

performed on the eve of the surgery. The period of preoperative preparation ranged from two to five days.

All patients were intubated with a double lumen endotracheal tube.

The position of the patient for the operation was the supine position with open arms. First the right hemithorax was approached, then the left. A metal arch was used to support the sternal elevator at the level of the sternal notch, raised to a height of 40 cm (Figure 4).

Two teams, one positioned at the head and the other on the right side of the surgical table, start the procedure (Figure 5).

The neck dissection was performed with an anterior transverse incision of about 5 to 8 cm, 2 cm above the sternal notch. Videothoracoscopy, first on the right and then on the left, was performed with three 10 cm trocars, two located between the midclavicular line and anterior axillary line in the 3rd and 6th intercostal spaces, and the other in the 5th intercostal space, in the anterior axillary line, with the removal not only of the thymus, but also of the pericardial fat and all of the perithymic tissue, bilaterally, as described in the surgical technique.[31] All the ressected tissues were removed through the cervical incision. During the operation, the right and left phrenic nerves were visualized and carefully preserved.

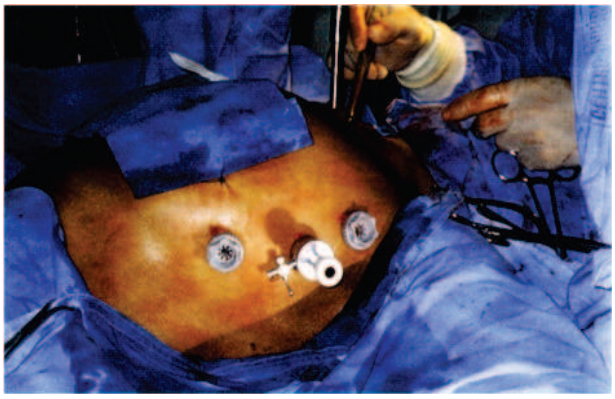

***Figure 4 -*** *Location of sternum lifter (cervicotomy) and trocars in the left hemithorax for thoracoscopy.*

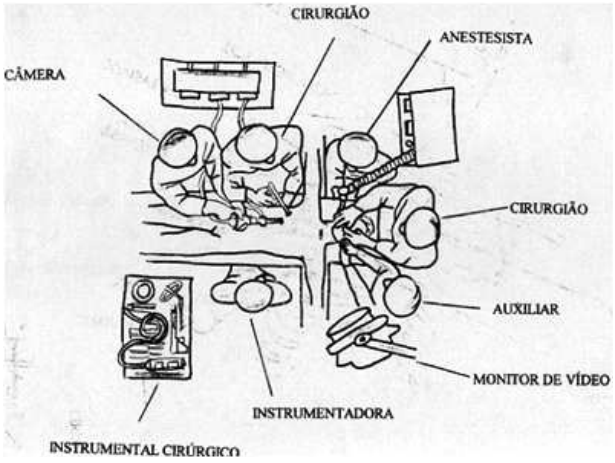


***Figure 5 -*** *Positioning of the two teams.*

There was no operative mortality. One (2.4%) conversion to a partial sternotomy was necessary due to the presence of considerable fat around the thymic tissue. This sternotomy was performed out of concern about leaving thymic remnants after videothoracoscopy. In this case with the open approach the left and right pericardial fat were easily resected.

Mean operative time was 210 minutes. Three (7.2%) patients required ventilatory support postoperatively and had extended (60, 30, and 15 day) stays in the intensive care unit (ICU), two complicated by pneumonia.

All other cases were extubated in the operating room, with the patient under observance for about 24 hours in the ICU or intermediate care unit. On average drains were removed two days after surgery. The mean number of postoperative days hospitalized was 7.6 days; the mean length-of-stay for the entire hospitalization was 12.6 days.

Pain was readily controlled with analgesics (acetaminophen or dipyrone) and non-steroidal anti-inflammatory drugs (NSAIDs), which were administered regularly during the first two days of the postoperative period. This analgesia regimen was provided to all patients, associated with blockage of the intercostal nerves with Bupivacaine 0.5% adjacent to the trocar orifices.

Seven patients experienced dysphonia the first few days postoperatively, which gradually improved in five and persisted in two patients (4.8%). In these two patients laryngoscopy showed left vocal cord paralysis with partial improvement of dysphonia after speech therapy sessions. In those who experienced only transient dysphonia laryngoscopy was not performed.

There were two (4.8%) vascular lesions, which occurred during neck dissection. One injury was to the innominate artery at the end of the operation that required sternotomy for the repair. This patient had undergone previous suprasternal thymectomy and

there were many adhesions in the tissues as well as the presence of residual thymus; there was no clinical improvement. After this case, we no longer recommeded videothorascopic surgery for the resection of residual thymic tissue. The other injury was of the left internal thoracic vein, which was repaired via neck incision.

Two (4.8%) patients presented alterations in coagulation after plasmapheresis with the presence of a large left intrapleural clot and another with hemothorax requiring bilateral drainage. The patient with the large clot was treated with 1,500,000 U intrapleural streptokinase administered through the chest tube, with significant reduction of the clot, no additional surgery was required. The other patient with hemothorax had to be re-operated. Diffuse bleeding from the resection area was encountered, requiring transfusion of clotting factors to treat the coagulopathy, with a satisfactory evolution. In these two patients plasmapheresis has been performed without replacement of plasma. Replacement of plasma was performed in the remaining patients who underwent preoperative plasmapheresis with part of the replacement after removal of the plasma filtrate. This fact makes us emphasize the need for fluid resuscitation in the plasmapheresis, not only albumin, but also with plasma.

The first day after surgery all patients resumed the medication previously used for the control of Myasthenia Gravis.

The postoperative care – which in our cohort ranged from 1 to 190 months – followed MGFA guidelines. There was one (2.4%) death attributed to the MG (D of MG), while the other 97.6% enjoyed better control of myasthenia gravis disease – (I) improved (CSR, PR, or MM). The patient who died had a myasthenic crisis triggered by urinary tract infection and died during the fourth postoperative month. This patient had undergone VATET *after* transcervical thymectomy with the finding of thymic tissue remnants.

Surgical specimens were sent to pathology separated: thymus, right pericardial fat, left pericardial fat, and other perithymic tissue when present. The thymus was so rigorously separated from the pericardial fat with the capsule intact that no cases were observed with fragmentation of the gland with the pericardial or perithymic tissues.

The histopathological results of the 42 patients who underwent VATET were: thymic hyperplasia (55.2%), thymic involution (24.0%), normal thymus (16.8%), and two (4.8%) thymomas (one encapsulated and the other with microscopic invasion of the capsule). A finding of great interest in histopathology was the presence of ectopic thymic tissue (not being a fragmentation of the gland) in seven (16.8%) patients. Six had it in the left pericardial fat, and one in the right and left pericardial fat and in the cervical region (Figure 6).

## FINAL CONSIDERATION/THOUGHTS

Thymectomy by VATS has been performed increasingly, as the results presented by various authors demonstrate similar efficacy to those performed by conventional surgery, with the advantages associated with minimally invasive surgery. The technique of extended thymectomy by VATS described offers a triple view – cervical, and right and left intra-thoracic – and the confidence that resection not only of the entire thymus but also of the perithymic tissues can be performed without the need for total sternotomy. Similar to other procedures performed by video-surgery, the standardization of the technique is very important, and as one performs more procedures the safety and the efficacy are consolidated.

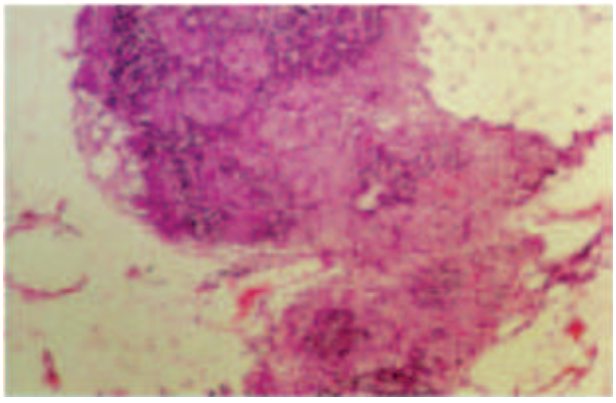

***Figure 6*** *- In the midst of pericardial fat, presence of thymic tissue (40x).*

**RESUMO**

A vídeocirurgia veio proporcionar mais uma alternativa de se realizar a ressecção do timo no controle da Miastenia Gravis com uma cirurgia minimamente invasiva. É nítido observar um crescente número de publicações de grupos de cirurgiões que aderiram a esta técnica, trazendo informações valiosas de seus resultados. O presente artigo traz um resumo das diferentes técnicas da timectomia video-assistida com seus resultados e também descreve a técnica utilizada pelos autores do trabalho e casuística.

**Descritores:** Cirurgia torácica vídeo-assistida, cirurgia torácica, *miastenia gravis*, timectomia.

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**Brazilian Journal of Videoendoscopic Surgery**

*Case Report*

# Portal Vein Injury in a Patient Undergoing Video-Assisted Cholecystectomy: Case Report and Review of Literature

## Lesão da Veia Porta em Paciente Submetido à Colecistectomia por Videolaparoscopia: Relato de Caso e Revisão da Literatura

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**ABSTRACT**

The laparoscopic approach has been recognized as a standard of excellence for cholecystectomy, one of the most frequently performed procedures in the world. We report an unusual case of damage to the portal vein in patients undergoing laparoscopic cholecystectomy and monitor the clinical evolution of patients with documentation of new clinical events. We performed a MEDLINE search using the following keywords: "portal venous injury" and "laparoscopic cholecystectomy". We identified in the literature few case reports of injuries of the portal vein or its branches in this procedure. Vascular lesions are not rare; however, particularly those affecting the portal vein during this procedure are uncommon, which justifies the publication.

**Key words:** portal vein; cholecystectomy, laparoscopy; complications.

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## INTRODUCTION

Gallstone disease is one of the most frequent pathological conditions of the digestive system, leading the incidence of diseases of the liver and bile ducts.[1] It affects approximately 25% of women and between 10% and 15% of men over 50 years of age.[1] Because minimally invasive surgery offers to less suffering, decreased metabolic imbalance, and faster recovery, this approach has become widely and enthusiastically adopted.[2,3]

Injury to the bile ducts is an important complication that may lead to death owing to peritonitis and biliary sepsis. The principal associated morbidities are benign biliary stenosis, cholangitis, secondary biliary cirrhosis, portal hypertension and liver failure. Injury to the bile ducts and vascular injury significantly contribute to morbidity and mortality. Depending on the degree of liver damage, liver resection, and even liver transplantation may be necessary.[4,5,6.]

Because the right hepatic artery frequently runs close and parallel to the cystic duct, it is especially vulnerable to injury, chiefly if the structures of the Calot's triangle are not clearly identified.[6] Most problems arise when the anatomical distribution is altered. Such anatomical alterations may be due to inflammation or another pathology such as a tumor, and is even more likely when inflammation is superimposed on anatomical variations of the hepatoduodenal ligament and hepatic hilum.[7]Ouvir

We report a rare case of portal vein injury in a patient undergoing video-assisted cholecystectomy, and compare it with other cases reported in the literature.

## CASE REPORT

The patient was a 49-year-old white male from Rio de Janeiro, who had multiple small gallbladder stones, and a history of several episodes of biliary colic. Complete blood count, hemostasis and thrombosis screening, serum glucose and serum thyroid-stimulating hormone (TSH) were normal. Operative risk being was graded as level I. The patient was then referred for video laparoscopic cholecystectomy. Upon trocar insertion, and upon release of loose adhesions

connecting the epiploon to the gallbladder unusually intense bleeding was noticed through the ports. There was a second, firm adhesion from the anterior wall of the duodenal bulb to the inferior aspect of the liver, anterior to the hepatic pedicle, hampering access to the latter. The cautery (Hook) was used to release this adhesion, with massive non-pulsatile dark bleeding, compatible with a venous origin, developing near the end of the procedure. Wide right subcostal laparotomy was performed immediately to access the hepatic pedicle.

There was massive bleeding from an anomalously positioned portal vein, hidden in the duodenal-hepatic adhesion. The bleeding was controlled with a Satinsky clamp and suture. A cholecystectomy according to the standard technique was subsequently performed. Because there was minimal bile extravasation from the confluence of the hepatic ducts, we opted for the placement of a Penrose drain, with suture of the abdominal wall. Some minutes later, however, while the patient was still on the operating table, there was massive bleeding from the abdominal wall, with formation of a large hematoma, with little blood flow though the Penrose drain. Another laparotomy identified a small volume of diffuse bleeding at the hepatic pedicle. Compressive hemostasis was performed with two large bandages placed in the subhepatic region, along with the placement of a Kehr's T-drain due to the bile extravasation. Only the skin was sutured, and another laparotomy for bandage removal, hemostasis and bile extravasation revision, and definitive closure was scheduled for 48 hours thereafter. During this repeat laparotomy, no more bleeding or bile extravasation were observed, and the wall was closed in planes. The patient was admitted to the intensive care unit, where he required mechanical ventilation for 12 days, due to pulmonary edema and respiratory failure upon extubation. During the surgery and the postoperative period, he received 5 units of blood. While in the ICU, there was marked leukopenia (< 2,000 leukocytes/ $mm^3$), and he received empiric antibiotics, although no bacterial infection was recognized. An anti-HIV ELISA was positive. The abdominal drain was removed one week after the surgery, and the Kehr's T-drain was kept in position. On the 14$^{th}$ postoperative day, a cholangiography performed through the Kehr's T-drain identified residual choledocholithiasis. The patient underwent endoscopic retrograde pancreatography (ERCP), with papillotomy and removal of the stones. The Kher's T-drain was removed and the patient was discharged.

## DISCUSSION

Laparoscopy results in more injury to the bile ducts than the open procedure. Studies comparing both approaches found a large vascular injury in 0.044% of the laparoscopic procedures, compared to 0.0% of the open approaches, and visceral injury in 0.07% of the laparoscopic procedures compared to 0.05% of the open approaches. [4,5,6,8] Moreover, bile duct injury during laparosopic cholecystectomy more frequently consists of complete transection, and thus is more serious than the injury occurring during open surgery. [4]

Access to the peritoneal cavity is the most delicate step; fatal complications are often related to needle and trocar insertion.[8] Because complications during primary access have not been significantly reduced, in spite of improvements in technology and surgical skills, several techniques aimed at preventing injury have been described. [8] Pneumoperitoneum, perhaps the most frequently of these techniques, has a mortality rate up to 0.2%. Injury to the bile ducts may be fatal or lead to long-lasting morbidity, increasing treatment costs or prompting litigation. [8]

The main causes of iatrogenic vascular injury are related to anatomical misidentification, thermal injury, inadvertently displacing clips, or excessive manipulation of the common biliary duct. Large vascular injury generally happens during dissection of the Calot's triangle, where the portal vein or right hepatic artery are closely related to the biliary tract, and susceptible to accidental injury or clipping.[1,9]

We conducted a search of the MEDLINE databank/database, using the terms: "portal venous injury" and "laparoscopic cholecystectomy", and identified several case reports of injury to the portal vein or its branches in patients undergoing videolaparoscopic cholecystectomy.

There is a wide variation in the incidence rates of vascular injury due to laparoscopic cholecystectomy, as reported from different studies. CHAPMAN *et al*[10] reported injury to the hepatic artery and/or portal vein in 28 (21%) of 132 patients, with injury to the biliary duct, whereas BACHA[11] reported 4.9% of vascular injury caused by laparoscopic cholecystectomy.[11] A recent study from the Northwestern University Medical School[12] reported

vascular injury in 71% of Bismuth level 4 patients, and in 63% of Bismuth level 3 patients.[11] The incidence rates of injury during laparoscopy to the main vascular elements – including the aorta, iliac vessels, inferior vena cava, mesenteric arteries and lumbar arteries – range from 0.07% to 0.4%, whereas the incidence rates of injury to minor vessels (branches of the epigastric, mesenteric and omental vessels) range from 0.1% to 1.2%.[13] Mortality rates range from 0.05% to 0.2%.[13]

BUELL *et al*.[14] reported the following complications: sepsis, infection of the surgical wound, relapsing cholangitis, and the need for prolonged ventilation. In a univariate analysis, arterial injury *versus* no arterial lesion was a predictor of mortality (38% vs 3%).[14]

GADZIJEV[7] reported injury to the common biliary duct and portal vein in a 38-year-old female during open right adrenalectomy, and injury to the common biliary duct in a 73-year-old male undergoing laparoscopic cholecystectomy. Both patients underwent liver transplantation.[7] RAGOZZINO et al.[5] reported two cases of laparoscopic cholecystectomy. The first case was a 39-year-old female with gallstones, in whom there was complete occlusion of the right hepatic artery immediately distal to the origin of the gastroduodenal artery, and occlusion of the right portal branch. The second case was a 36-year-old female with cholelithiasis and occlusion of the right hepatic artery and portal vein, caused by a surgical clamp.[5]

FIELDS et al.[15] reported the need for conversion to open laparotomy when laparoscopy revealed considerable inflammation of the gallbladder and surrounding structures, with excessive bleeding in the cystic area, and injury to the common biliary duct, in a patient with agenesis of the right hepatic lobule.[15] FELEKOURAS *et al*.[6] also reported the need for conversion to open laparotomy in a 75-year-old male with acute cholecystitis, due to severe inflammation and dense adhesions in the Calot's triangle, with bleeding due to injury to the portal vein obscuring the surgical field.[6]

In this case, the presence of firm grip extending from the anterior wall of the duodenal bulb to the underside of the liver in hepatic-duodenal region, resulted in the inability to access or visualize the portal vein since it was subsumed in the adherence and displaced forward in relation to its normal anatomical position. This situation led to the injury of this vascular structure.

## CONCLUSION

Vascular injury during laparoscopic cholecystectomy, not so uncommon, may be serious, generating grave complications and putting the patient's life at risk. Therefore, adequate monitoring and early diagnosis are necessary, as a change in the surgical approach can correct the injury and reduce morbidity and mortality.

**RESUMO**

A via laparoscópica tem sido reconhecida como padrão de excelência para a colecistectomia, sendo um dos procedimentos cirúrgicos mais realizados no mundo. Relatamos um caso incomum de lesão de veia porta anteriorizada em paciente submetido à colecistectomia videolaparoscópica e acompanhamos a evolução do paciente com registro dos novos eventos clínicos. Foi realizada uma pesquisa no MEDLINE utilizando as seguintes palavras-chave: "portal venous injury" and "laparoscopic cholecystectomy". Identificamos na literatura poucos relatos de casos associados à lesão da veia porta ou seus ramos neste procedimento. Lesões vasculares não são raras, porém, especificamente as que acometem a veia porta durante este procedimento são incomuns, o que justifica sua publicação.

**Descritores:** veia porta; colecistectomia laparoscópica; complicações.

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**Brazilian Journal of Videoendoscopic Surgery**

*Case Report*

# Technical Aspects of Laparoscopic Cholecystectomy in a Patient with *Situs Inversus Totalis* – Case Report

## Aspectos Técnicos da Colecistectomia Videolaparoscópica num Paciente com *Situs Inversus Totalis* - Relato de Caso

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**ABSTRACT**

*Situs inversus* is a rare anomaly characterized by transposition of organs to the opposite side of the body. We report a 16-year-old woman with known *situs inversus* totalis and gallstone disease who underwent a successful laparoscopic cholecystectomy. Diagnostic and technical challenges of the operation are discussed.

**Key words:** *Situs inversus totalis*, Laparoscopic cholecystectomy, Gallstone Disease.

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## INTRODUCTION

*Situs inversus* is a autosomal recessive morphogenetic abnormality, characterized by the transposition of the abdominal viscera to the opposite side.[1] This inversion of the topography can occur in the abdominal cavity *and* the chest or, more rarely, in one of the two. Its incidence is estimated at 1:5,000 to 1:20,000 live births.[2] The clinical diagnosis of gallstones in these patients is more difficult because the clinical presentation is confusing, especially because of the pain localized to the left hypochondrium. There is no evidence showing a higher incidence of gallstones in people with *situs inversus* than in those with the orthotopic topography of the abdominal viscera.[2] Several studies have shown that laparoscopic cholecystectomy is safe in these patients, however, due to the rarity of this condition, there is no standardization of procedure's technique.[1-5] Our objective is to present the case of a women with *situs inversus* and cholelithiasis who underwent laparoscopic cholecystectomy and discuss the technique used.

## CASE REPORT

The patient was an overweight (BMI = 26.9) 16 year old adolescent female with an established diagnosis of *situs inversus totalis*, who presented with a four month history of biliary colic, that localized to the left hypochondrium. Chest radiograph, electrocardiogram, and ultrasound revealed dextrocardia, sinus rhythm and *situs inversus totalis* with the presence of multiple gallstones with an average diameter of 6 mm.

The laparoscopic cholecystectomy was performed with the patient in the semi-lithotomy position with the surgeon between patient's legs. The trocars were positioned as shown in Figure 1. After the optic was introduced, the mirrored anatomy of the abdominal organs was noted (Figure 2).

The surgeon maneuvers his instruments through the pararectus trocars and performs the dissection of the infundibulum with the right-hand forceps while both the Assistant surgeon on the right and the Assistant surgeon on the left of the patient pull the bottom of the gall bladder postero-superiorly

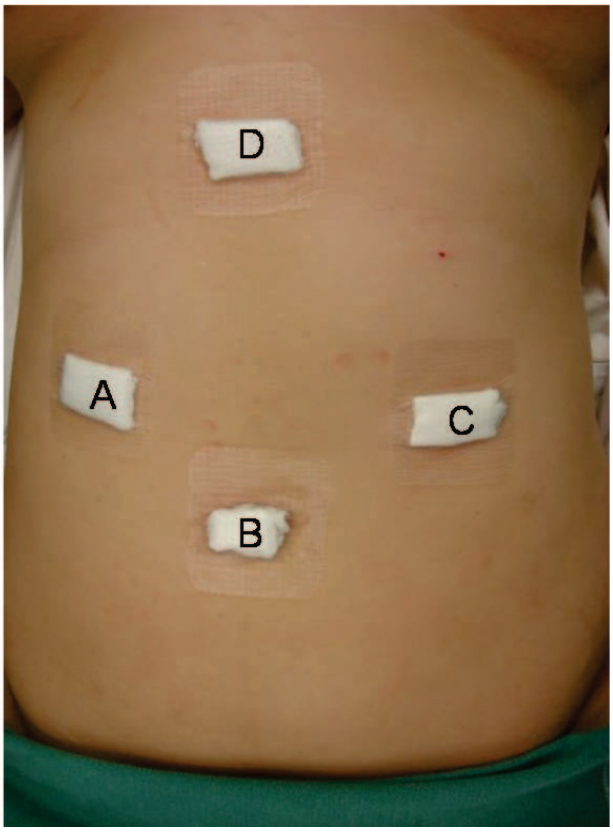


***Figure 1 –*** *Dressings corresponding to the trocar positions. A) Right Pararectus (10mm); B) Umbilicus (10mm); C) Left Pararectus (5mm); D) Epigastric (5mm).*

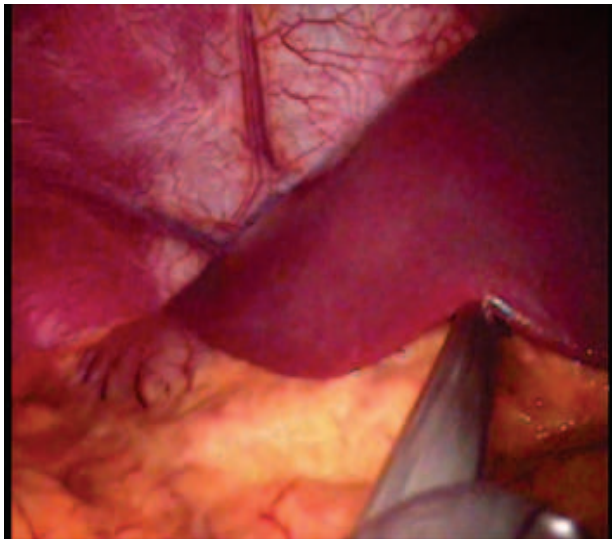

***Figure 2 –*** *Videolaparoscopic view of the mirrored anatomy of the abdominal organs.*

through trocar placed adjacent to the xiphoid process while the Assistant surgeon on the right of the patient maneuvers the camera. Cholangiography was performed intraoperatively (Figure 3) to identify anatomical variations of the biliary tree; none was noted. After 90 minutes of surgery the gallbladder was removed through the umbilicus. The patient was discharged the next day.

## DISCUSSION

In 1600, Fabricius described the transposition of the abdominal organs in a man.[5] The first report of a laparoscopic cholecystectomy in a patient with *situs inversus* was published in 1991.[5] Although it is a condition in which there is an alteration of the anatomy, there is no predisposition to gallbladder disease.

The technical challenge performing a laparoscopic cholecystectomy in a patient with inversion of the abdominal organs – when confronted with the mirror image – consists in adapting the position of the surgeon, the Assistants, and the trocars for the dissection of the gallbladder hilum and the exposure of the gallbladder.

Most reports in the literature describe the mirrored arrangement of both the trocars and the surgical team[1,3,5] corresponding to the inversion of the abdominal organs. This positioning, which at first seems more logical, accentuate the cognitive bias and hampers the dissection of the Calot's triangle. The surgeon is not accustomed to seeing the falciform ligament crossing superiorly and to the left across the video screen. There is constant crossing of the instruments as the base of gallbladder is brought forward, a frequent need for dissection with the left hand,[4] and even placement of an extra trocar.[2] In this context it was suggested that laparoscopic cholecystectomy would be more easily performed by a left-handed surgeon.[4]

When operating between the legs of the patient, the adaption to the inversion of the position of the intracavitary organs seems faster. The surgeon performed the dissection of the gallbladder hilum with his right hand in the region anterior and posterior to Cabot's triangle (Figure 4) and there were no crossing of the instruments. The camera and the forceps adjacent to the xiphoid were handled by both the first and second Assistant surgeons as needed during the surgeon's dissection. The placement of clips and the sectioning of the cystic duct were performed with the surgeon's left hand, while the catheter for cholangiography was inserted with the right hand. If a 10mm trocar is placed in the left flank, the surgeon

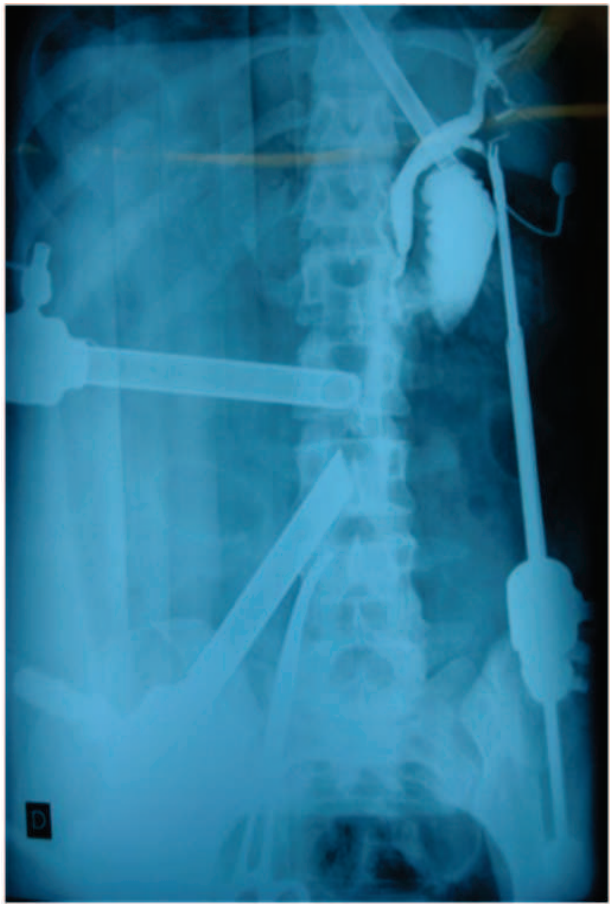

***Figure 3 -*** *Intra-operative Cholangiography.*

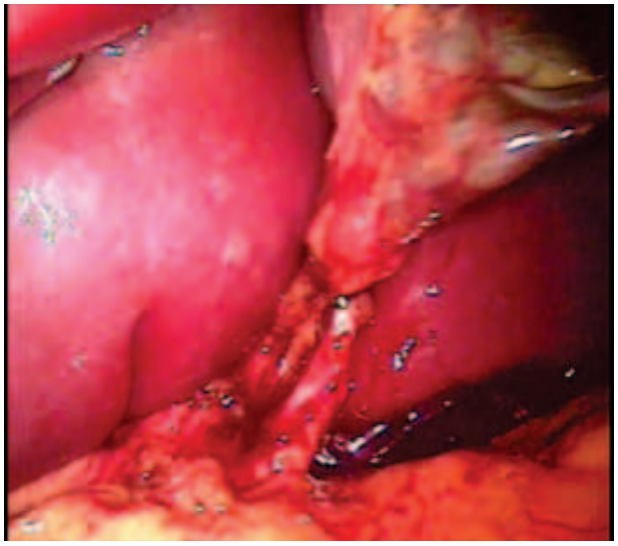

***Figure 4 -*** *View of Calot's Triangle.*

could clip and section the structures exclusively with the right hand.

We conclude that laparoscopic cholecystectomy in patients with *situs inversus totalis* has advantages when performed by the technique described above, since it avoids crossing of the instruments and permits the dissection with the right hand, facilitating the adaptation to the cognitive bias associated with the inversion of the abdominal organs.

**RESUMO**

*Situs Inversus* é uma anomalia rara caracterizada pela transposição dos órgãos para o lado oposto. Neste relato de caso apresentamos uma paciente com diagnóstico de situs inversus totalis e colelitíase, sendo submetida, em nosso serviço, a uma colecistectomia videolaparoscópica bem sucedida. As dificuldades diagnósticas e técnicas da cirurgia são discutidas.

**Palavras-chaves:** *Situs Inversus Totalis*, Colecistectomia videolaparoscópica, colelitíase.

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# INFORMATION FOR AUTHORS

**1. Objectives**

BRAZILIAN JOURNAL OF VIDEOENDOSCOPIC SURGERY (BJV) is the official journal of the Brazilian Society of Videosurgery that publishes scientific articles in order to register results of videosurgery researches and related subjects, encourages study and progress in this area as well as publications to deepen medical knowledge.

**2. Analysis, Selection and Exclusiveness of Manuscripts**

Manuscripts submitted will be analyzed by a Reviewers Committee, the manuscripts should be original and should not be published elsewhere. A copy of the manuscript is anonymously forwarded by the Editor to 2 or 3 reviewers to be analyzed within 30 days.

Peer review includes suggestions to the Editor, reject or accept the manuscript with or without changes. Manuscripts that are rejected will be returned to the author. Afterwards, peer review suggestions are forwarded to the main author for approval who will decide if she/he will resubmit it. Scientific articles describing experiments on human subjects or animals must include approval of the appropriate ethics committee of the institution where the study was performed, in accordance with the Declaration of Helsinki (1964 and 1975,1983 and 1989 amendments), the Animal Protection International Rules and the National Health Council Resolution nº 196/96. Republishing a national or an international journal article is only accepted in special cases and must be accompanied by written permission for its use from the copyright owner and the author. In this case a copy of the first manuscript version should be provided. Manuscripts must have up to 6 authors in order to be published.

**3. Periodicity & Scientific Matters to be published**

Brazilian Journal of Videoendoscopic Surgery is published quarterly. It is a communication channel of scientific matters such as:

- Original Article: original clinical(or experimental) research;
- Preliminary Communications: partial results on new researches, techniques and methods in study;
- Case Report(or Clinical Meeting): with critical analysis and discussion;
- Clinical Observation: should have critical analysis and discussion;
- Epidemiologic Statistics: with critical analysis and discussion;
- Description and Evaluation: of methods or procedures, with revision, critical analysis and discussion;
- Opinion and Analysis: of philosophical, ethical and social aspects regarding the area of study;
- Letters to the Editor: including criticisms and suggestions about publications, as well as questions and/or comments about manuscripts that have already been published.

**4. Requirements for preparation and submission of manuscripts**

Authors should send the manuscript in microsoft word format by email to: revista@sobracil.org.br). Security Copy: A copy of all materials submitted to the journal will be sent to the author with the approval by the Editorial Board for future copyrights warranties. IMPORTANT! Keep a copy of all the material submitted to the publication of your manuscript.

**Cover letter**: A cover letter signed by the main author should be enclosed. If the author have interest in pay for colored illustrations this should be specified in the cover letter.

**Permission for reproduction and copyright transfer statement:** Manuscripts must be accompanied by written permission for use of copyrighted material or photographs of identifiable persons. Copyright transfer statement must be sent.

**Protection sending the manuscript**: Manuscripts should be sent in a suitable package, in order to avoid bending photographs and illustrations.

**5. Standard Format and Print out**

- Manuscripts should be typed double-spaced with up to 25 lines per page.
- Pages should be numbered consecutively (numbers should be in the upper or lower right corner). The first page should be the Title Page.
- Each section should start on a new page.
- Manuscripts should be printable on one side of a 216x279mm or A4(212x297mm) white sulphite paper with margins of 25mm.
- Manuscripts should include, in sequence and on separate pages:

- Identification Page (Title page – see details bellow);
- Abstract/Key words;
- Text pages and Acknowledgments;
- References;
- Tables (one in each page, separately);
- Illustrations;
- Legends;
- Abbreviations.

**6. Manuscripts Preparation**

*6.1. Identification Page (Title Page)*

All manuscripts will be subject to a process of anonymous editorial review, therefore the name and address of authors should only be in the Title Page with identification as it is not going to be sent to the reviewers. The authors should verify if there is any identification on the text to avoid identification.

**Title Page "without identification"**

- Complete Manuscript Title(concise and informative)
- Short title ( up to 8 words)

**Title Page "with identification"**

- Name(s) of author(s) and Institutional Scientific Affiliation: provide detailed information about the department and the institute where the work was conducted. Affiliation and/or Academic degrees of the authors: include name, highest academic degree and institutional affiliation and position of each author.
- Footnotes:

Address, telephone, fax and e-mail of the main author should be given for journal editor contact.

Address to request copies and to contact author (include full address information and e-mail of the author who submitted the material to be published).

- Source of Funding: it should be declared any source of funding such as grants, equipments and others.

*6.2. Abstract*

The abstract is mandatory. It should be up to 250 words. Every abstract should be written in an informative style. Depending on the abstract it should contain the following headings:

**Original Articles**: Objectives/Materials(Patients) and Methods/Results/Discussion/Conclusion(s).

**Reviews, Actualization, Opinion**: Objectives/History(Scientific Summary)/Discussion

**Case report or Clinical Meetings**: Objectives/Meetings Summary/Discussion

**Technical Notes or Preliminary Communication**: Objectives/Technical Report/ Research Report/ Preliminary Results/Discussion

*6.3. Descriptors (Key Words)*

Identify the manuscript with 3 to 10 key words or short phrases bellow the abstract using DeCS or MESH terminology which will assist indexers in cross-indexing the article in the data base.

For DeCS terms access: **http://decs.bvs.br** and for MESH (Medical Subject Index) terms access: **http://www.nlm.nih.gov/mesh/meshhome.html** . If suitable MeSH terms are not yet available, well known terms or expressions are accepted.

*6.4. Text*

The textual material of clinical or experimental observation manuscripts should be organized whenever possible in a standard form as follows: Introduction, Patients and Methods, Results, Discussion, Conclusion, Acknowledgment, References. Other types of manuscripts such as case report, editorials and reviews may follow a different format, according to the Editorial Board. Long manuscripts in order to provide a better understanding of its contents may include subheadings in some sections such as Results and Discussion.

**Citations and References:** Authors citations must appear in the text as superscript numbers placed to the right of a word, sentence or paragraph. Citations of names should be typed in Upper Case. Name of author(s) citation should follow the format bellow:

- One author: KOCK[1]
- Two authors: KOCK e PENROSE[1]
- Three or more authors: KOCK and cols. [1]

Note: In the body of the text the form "…and cols" is suggested and in the references "… et al".

**Introduction** – It should briefly describe the reason to accomplish the article and the objective. Do not include data or conclusions and mention only relevant references.

**Materials (or Patients) and Methods** – should describe in detail the recruitment of individuals (human subjects and laboratory animals as well as group control) included in the research. Identify the age, sex and other relevant characteristics of the subject. Authors should be careful when specify race or ethnic group as their definition and relevance are ambiguous. Methods, apparatus (with manufacturer's name and address in parentheses) and procedures used should be identified in adequate detail so that other researches can reproduce the experiment. The methods published in other research should be mention and unknown methods briefly described. Statistical methods and protocols used should also be described, as well as the computers software used. Authors that submitted reviews should include a section to describe the methods used for locating, selecting, extracting and synthesizing data. These methods should be summarized in the abstract. When the paper reports experiments on human subjects it must indicate whether the procedures followed ethical standards of the responsible committee on human experimentation. Do not use name, initials or hospital identification of the patients, especially in illustrative material. When the paper reports experiments on animals, it must indicate that protocols were reviewed by the appropriate institutional committee with respect to the care and use of laboratory animals used in this study.

**Results** – Provide results in a logical sequence in the text, tables and figures. Do not repeat all tables and figures data in the text; consider the relevant ones.

**Discussion** – Emphasize important and new aspects of the study as well as the conclusions originated from them. Avoid detailed repetition of the data provided in the Introduction or Results. Include findings implications and limitations in the Discussion Section, mentioning implications for future research. Compare what was observed to other relevant studies.

**Conclusions –** The conclusions should be based on the study objectives, in order to avoid unqualified statements and conclusions that are not based on the findings. Author(s) should not state the economic benefits and costs unless their manuscript includes economic analysis and data. Studies that have not been completed should not be mentioned. New hypothesis should only be considered if justified. Include recommendations when appropriate.

**Acknowledgement:** Acknowledgements to people and institutions may be included at the end of the manuscript, stating any type of contribution and/or participation towards the development of the research. Technical support should be acknowledged in a paragraph separate from other types of contributions.

*6.5. References*

The references that are stated in the text should be consecutively in alphabetical order or as they are cited in the text. References, tables and legends must be identified in the text by superscript Arabic numerals. Citation of manuscripts accepted but not yet published: mention the journal and add "In press" in the reference list (authors should have written permission to mention these articles, as well as to verify if manuscripts were accepted to publication).

Avoid personal communications citation, unless it provides essential information and it is not possible to be obtained in printed sources (in such case they should be cited in parentheses in the text with name of the person and date of the communication). The Brazilian Journal of Videoendoscopic Surgery is in accordance with "Vancouver Style" (uniform requirements for manuscripts submitted to biomedical journals), electronic version is available on **http://acponline.org/journals/annals/01jan97/unifreqr.htm**, also published in N Engl J Med 1997; 336(4): 309-315 and commended by the International Committee of Medical Journal Editors.

The Uniform Requirements (Vancouver Style) are based on the American National Standards Institute (ANSI) adapted by the NLM (National Library of Medicine). Complete information about format of references may be verified in: Uniform Requirements for Manuscripts, Journal of Public Health 1999; 33(1), also available in electronic version: http:// www.fsp.usp.br/~rsp: http:// www.fsp.usp.br/~rsp.

Examples of references format:

- **Periodical article**

Include only the first 6 authors and add "et al". Do not use Upper Case or bold or underlined or italics. Journal names are abbreviated according to the Index Medicus – in the List of Journals Indexed in Index Medicus available at **http://www.nlm.nih.gov/tsd/serials/lji.html**, and the Latin American Journals available at: **http://www.bireme.br/abd/P/lista_geral.htm**.

Ex: Parkin DM, Clayton D, Black RJ, Masuyer E, Friedl HP, Ivanov E, et al. Childhood leukemia in Europe after Chernobyl: 5 years follow-up. Br J Cancer 1996; 73: 1006-12.

- **Book**

Ex: Rigsven MK, Bond D. Gerontology and leadship skills for nurses. 2nd ed. Albany (NY): Delmar Publishers; 1996.

- **Chapter in Book**

Ex: Philips SJ, Whiosnant JP. Hypertension and stroke. In: Laragh JH, Brenner BM, editors. Hypertension: pathophysiology, diagnosis and management. 2nd ed. New York; Raven Press; 1995. p.465-78.

- **Conference Paper**

Ex: Bergtson S, Solhein BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editor. MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sep 6-10; Geneva, Switzerland, Amsterdam: North Holland; 1992. p.1561-5.

- **Dissertation**

Ex: Carvalho ACP. A contribuição da tomografia computadorizada ao diagnóstico de aneurisma dissecante da aorta [dissertação - mestrado]. Rio de Janeiro: Faculdade de Medicina, Universidade Federal do Rio de Janeiro; 1993.

Kaplan SJ. Post-hospital home health care: the elderly's access and utilization [dissertation]. St. Louis (Ø): Washington Univ.; 1995

- **Journal article in electronic format**

Ex: Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis [periodical online] 1995; 1(1). Available from: URL: http://www.cdc.gov/ncidod/EID/eid.htm [consulted on 11/12/2002].

- **Opinion or technical articles online**

Ex: Carvalho ACP, Marchiori E. Manual de orientação para a elaboração de monografias, dissertações e teses. Avaialabre from: URL http://www.radiologia.ufrj.br/manual.htm [consulted on 08/12/2002].

*6.6 Tables*

Print out each Table on a separate sheet of paper. Number tables with Arabic numerals consecutively in the order of their first citation in the text and supply a brief title for each table. Data that are shown in the table should not be repeated in the graphics. Follow the "Guidelines for Tabular Presentations" established by the National Statistical Council (Rev Bras Est 1963, 24:42-60). Explanatory matter in the footnotes of the tables should be limited and the following symbols should be used in this sequence */+/§/**/§§ etc. Identify the statistical analysis of dispersion such as standard deviation and standard error of the mean.

*6.7. Illustrations (figures, drawings, graphics etc.)*

Illustrations should be numbered with Arabic numerals consecutively according to the order in which they have been first cited in the text, they should be mentioned as "Figure". All photographic documentation should have on its back (in pencil) the number of the legend and page in the text indicating the correct position(portrait or landscape) of the figure, that may be glued on a separate sheet of paper. Illustrations (drawings or photographs without mounting) should not be larger than 203x254mm. Legends should be in a separate sheet of paper. The illustrations should allow a perfect reproduction of the original. Drawings and graphics should be done with nankim ink in white paper or drawing paper, and normographe fonts should be used for lettering, freehand and typewritten lettering is unacceptable. High resolution digital photographs printed in high quality photographic paper will be accepted. Copies of the digital photographs should be submitted on BMP, JPEG or TIFF format in CD or diskette. Colored photographs will not be accepted for publication in black and white. Illustrations in color require in real color for reproduction whenever possible.

**Legends for Illustrations**

Print out legends for illustrations using double spacing, on a separate page, with Arabic numerals corresponding to the illustrations. When symbols, arrows, numbers, or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend. Explain the internal scale and identify the method of staining in microphotographs.

*6.8 Abbreviations*

Use only standard abbreviations, avoiding abbreviations in the title and abstract. The first time an abbreviation appears it should be preceded by the full term for which an abbreviation stands in the text, unless it is a standard unit of measurement.

**7. Protection of Patients' Rights to Privacy** - Information that may identify a patient as a subject of a study (descriptions, photographs, and genealogy) should not be published without patient's informed consent. Photographs with inadequate protection of anonymity may be rejected by the publisher, if patients' rights to privacy were infringed. In these cases, the journal publisher's may require patient's informed consent.

**8. Approval of Local Ethics Committee** – Authors should send a letter with approval of the appropriate local ethics committee signed by all of them or the main author when the study involves human beings.

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**12**. Brazilian Journal of Videoendoscopic Surgery editorial committee neither accept advertising nor pay authors of manuscripts published in its pages.

**13**. Brazilian Journal of Videoendoscopic Surgery reserves the right to reject manuscripts that do not comply with the requirements (presentation, typewrite, number of copies, copy in diskette, requested items …) in addition to suggest changes to manuscripts under the Editorial Board and Editorial Consultants analysis.

**14**. The Editorial Board when necessary will automatically adjust all approved manuscripts to the proposed requirements.

**15.** Conflict of interest disclosure statement: All authors must disclose any commercial interest, financial interest, and/or other relationship with manufacturers of pharmaceuticals, laboratory supplies, and/or medical devices and with commercial providers of medically related services. All relationships must be disclosed. Off label uses of products must be clearly identified.

**16.** Randomized controlled trial and clinical trials must be registered before submitted to publication. Instructions for registration can be found in **http://www.icmje.or/clin_trialup.htm** and the registration can be done in the National Library of Medicine clinical trial database (http://clinicaltrials.gov/ct/gui).

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# MANUSCRIPT CHECKLIST

The authors should observe the following checklist before submitting a manuscript:

☑ Send three paper copies of the article (including figures, tables and graphics with legends).

☑ Include one copy in a CD in Microsoft Word software, with figures, tables and graphics with legends or send the files by email to: Revista@sobracil.org.br

☑ Write: a) Manucript cover letter; b) Permission for reproduction (including authorization for reproducing and copyright transfer statement; c) Letter of Clinical Research Approval of the Institution Ethics Committee where the study was conducted.

☑ Include: Identification Page (Title Page "with identification"), with a complete title of the manuscript; name(s) of author(s) and affiliation (or title(s)): institution where the work was conducted. Address, telephone and e-mail of the main author. b)Title Page "without identification" with Complete Manuscript Title and Short title to be sent to the Editorial Board.

☑ Verify standards formats and print out (pages numbered consecutively, double-spaced, one side of the paper print out, etc…).

☑ Verify sequence of the headings of the sections (depending on the type of manuscript).

☑ In the Abstract include: Objectives, Material (or Patients) and Methods, Results and Conclusion(s). Check the key words. The Abstract should have 200-250 words.

☑ Check if the references are according to the journal requirements: numbered consecutively, in alphabetical order or following the sequence that they are mentioned in the text.

☑ Verify the Legend of the Figures, Graphics and Illustrations that should be on a separate page.

☑ Photographs and Illustrations should be sent in a high quality resolution for possible reproduction (colored photographs will not be accepted for publication in black and white). Identify the photography on its back (in pencil) the number of the legend and page).

**BRAZILIAN JOURNAL OF VIDEOENDOSCOPIC SURGERY** reserves the right to reject manuscripts that do not comply with the requirements (presentation, typewrite, number of copies, copy in diskette, requested items …) in addition to suggest changes to manuscripts under the Editorial Board and Editorial Consultants analysis.