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Colangiografias Intraoperatórias com Defeito de Enchimento: Análise Comparativa de Complicações da Manutenção Pós-operatória de Cateter Transcístico

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“Do you know what is the greatest gift anyone can receive in his lifetime?
The greatest gift we can receive is to have the chance to make a difference.”

Stephen V. Strange, M.D., Ph.D.

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RESUMO

Introdução: Esta é uma coorte retrospectiva de pacientes submetidos a colecistectomia videolaparoscópica com colangiografia intraoperatória (CIO) com achados sugestivos de coledocolitíase. Foi realizada análise comparativa da taxa de complicações para os pacientes que tiveram mantido cateter de colangiografia na sua posição transcística (TC) no pós-operatório. Esta é uma prática proposta para superar a limitada disponibilidade de colangiopancreatografia endoscópica retrógrada (CPRE), assim como evitar explorações cirúrgicas das vias biliares. **Materiais e Métodos:** Foram revisados retrospectivamente todos prontuários médicos de pacientes submetidos a CIO de janeiro de 2015 a dezembro de 2018. Dados demográficos e perioperatórios dos pacientes desde a internação na qual a colecistectomia ocorreu até a última visita ambulatorial foram comparados entre os dois grupos (com vs. sem cateter TC). Complicações foram classificadas usando a escala de Clavien-Dindo. **Resultados:** Análise univariada demonstrou um aumento de 2.4 vezes no risco de complicações (95%IC 1.13- 5.1) entre os grupos de comparação. O número de CPREs (18 vs. 30) não foi significativamente diferente entre manter ou não o cateter TC no pós-operatório, respectivamente. A análise estratificada seguida de regressão logística exata apoiou o achado que manter o cateter TC no pós-operatório aumentou a taxa de complicações (OR=5.34, 95%IC 1,22-29,83, p=0.022), ajustando para potenciais fatores de confusão. **Conclusão:** A manutenção do cateter transcístico no pós-operatório não se mostrou efetiva em significativamente reduzir o número de CPREs ou complicações associadas. Desfechos advindos da prática causaram eventos adversos que suplantaram potenciais benefícios. Mais ainda, acompanhamento expectante é razoável para pacientes com evidência de cálculos no ducto biliar comum. Não se recomenda a prática, mesmo no contexto de limitada disponibilidade de recursos mais modernos no manejo de coledocolitíase.

Palavras-chave: Coledocolitíase, colangiografia, cateter transcístico, complicações

ABSTRACT

Background: This is a *retrospective cohort* of patients undergoing laparoscopic cholecystectomy with intraoperative cholangiography (IOC) with suggestive findings for choledocholithiasis. A comparative assessment in complication rates was performed for patients that had their cholangiography catheter maintained in its transcystic duct (TCD) position postoperatively. This is a practice proposed to overcome the limited availability of Endoscopic Retrograde Cholangiopancreatography (ERCP) as well as to avoid surgical exploration of the common bile duct. **Methods:** Retrospective medical record review of all positive IOC from January 2015 to December 2018 was performed. Patients' demographic and perioperative data from the hospital stay period in which the cholecystectomy occurred until the last surgical ambulatory visit was compared between groups (with vs. without TCD catheter). Complications were operationalized using the Clavien-Dindo scale. **Results**: Univariate analysis of complications showed a 2.4-fold risk increase in complications (95% CI 1.13 to 5.1) between comparison groups. Number of ERCPs (18 vs. 30) were not significantly different between maintaining or not the TCD catheter postop, respectively. Stratified analysis followed by exact logistic regression supported the findings that maintaining the TCD catheter postoperatively increased complication rates (OR=5.34, 95% CI 1.22, 29.83, p=0.022), adjusting for potential confounders. **Conclusion:** The maintenance of the TCD catheter postoperatively did not prove to be effective in significantly reducing the number of ERCP nor associated complications. Also, outcomes inherited from the practice caused adverse events that surpassed its potential benefits. Moreover, expectant follow-up is reasonable for patients with evidence of common bile duct stones. We do not recommend this practice, even in settings where there are limited resources of more modern management of choledocholithiasis.

Key Words: Choledocholithiasis, cholangiography, transcystic duct catheter, complications

LISTA DE ABREVIATURAS

CBD	Common bile duct
CI	Confidence interval
CIO	Colangiografia intraoperatória
CPRE	Colangiopancreatografia retrógrada endoscópica
CRNM	Colangiopancreatografia por ressonância nuclear magnética
ERCP	Endoscopic retrograde cholangiopancreatography
EUS	Endoscopic ultrasound
GGT	Gamma glutamyl transferase
IOC	Intraoperative holangiography
MRCP	Magnetic resonance cholangiopancreatography
OR	Odds ratio
SUS	Sistema único de saúde
TC	Transcístico (a)
TCD	Transcistic duct
US	Ultrassom / Ultrassonografia

SUMÁRIO

1 INTRODUÇÃO

1.1 COLELITÍASE

A prevalência de cálculos biliares na vesícula biliar (colelitíase) é alta, e varia de acordo com a metodologia diagnóstica empregada e com a população estudada.(STINTON; SHAFFER, 2012) Nos EUA, cálculos estão presentes em aproximadamente 6% dos homens e 9% das mulheres adultos, representando 25 milhões de pessoas e resultando em mais de 600 mil colecistectomias por ano.(EVERHART *et al.*, 1999) No Brasil, a prevalência de cálculos identificados em adultos tanto por ultrassom como em necropsias é de aproximadamente 10% (9.3%-18.4%). (COELHO *et al.*, 1999; MANTOVANI *et al.*, 2001; TORRES *et al.*, 2005)

Mais de 90% dos cálculos biliares são compostos principalmente por colesterol e se formam na vesícula biliar. A formação dos cálculos é resultado de fatores fisiopatológicos (de etiologia genética e ambiental) como hipersaturação da bile por colesterol, hipomotilidade vesicular e trânsito intestinal lento que permitem que microcristais de colesterol sejam retidos e sofram nucleação. (PORTINCASA *et al.*, 2006) O restante dos cálculos biliares (< 10%) é composto por sais de cálcio polimerizados que se precipitam gerando cálculos pigmentados cuja fisiopatologia é diversa. Cálculos pigmentados apresentam maior prevalência de formação fora da vesícula biliar, diretamente nas vias biliares.

A maioria dos indivíduos com cálculos biliares são assintomáticos durante toda a vida e colelitíase representa um achado acidental. Destes, aproximadamente 15 a 25% se tornam sintomáticos após 10 a 15 anos de acompanhamento.(SHABANZADEH *et al.*, 2016) O sintoma mais comum de colelitíase é dor, classicamente em cólica e localizada no quadrante superior direito do abdome. A partir do momento em que um paciente inicialmente assintomático apresenta dor, o seu risco de desenvolver complicações é de 2-3% ao ano. (FESTI *et al.*, 2010) Dentre as complicações, destaca-se colecistite aguda como a mais comum, definida como a inflamação mural da vesícula biliar. A segunda complicação mais comum é a migração dos cálculos para a via biliar principal – definida como coledocolitíase.

1.1 COLEDOCOLITÍASE

A presença de cálculos no ducto biliar comum (ou ducto colédoco) caracteriza a coledocolitíase. O ducto colédoco é formado a partir da junção do ducto cístico e ducto hepático comum e representa a porção terminal da via biliar extra-hepática. Distalmente, entra em contato com o ducto pancreático principal, unindo-se a ele, e formando a ampola hepatopancreática (de Vater). A porção distal da ampola se abre no duodeno através da papila duodenal maior. Musculatura lisa esfincteriana (esfíncter de Oddi) controla a drenagem da bile, produzida pelo fígado e estocada na vesícula biliar, e das secreções pancreáticas para o intestino. (MOORE *et al.*, 2019)

A incidência de coledocolitíase varia de 8 a 18% em pacientes portadores de colelitíase sintomática. (KO; LEE, 2002) Estima-se que litíase na via biliar principal esteja presente no momento da colecistectomia em 5 a 20% dos casos. (DASARI *et al.*, 2013; GURUSAMY *et al.*, 2015; MANNING *et al.*, 2017) Quando a colecistectomia é realizada no contexto de colecistite aguda, a incidência de coledocolitíase é ligeiramente maior, aproximadamente 13,7% (11,8-15,9%). (CHEN *et al.*, 2019) Em países ocidentais, a maioria dos casos é secundária a migração de cálculos da vesícula biliar para o colédoco através do ducto cístico. Coledocolitíase primária (ou seja, formação de cálculos dentro do ducto biliar comum) é menos comum e geralmente ocorre em situações que predispõem a estase biliar. (ROHDE; OSVALDT, 2018)

Considerando a história natural do cálculo na via biliar, as complicações mais frequentemente associadas à coledocolitíase são a pancreatite e a colangite aguda. (MANNING *et al.*, 2017) A pancreatite aguda é a doença inflamatória do parênquima pancreático que, no contexto da etiologia biliar (a mais comum), ocorre pelo aumento da pressão no ducto pancreático. Isso gera hiperestimulação dos ácinos pancreáticos, refluxo ativo de tripsina, e subsequente ativação desregulada. A pancreatite aguda pode se apresentar como uma doença leve, moderada, ou grave, potencialmente fatal. (LIU *et al.*, 1997) A colangite aguda se caracteriza por uma síndrome clínica cuja fisiopatologia se relaciona a estase e infecção ascendente da via biliar. A causa mais frequente (28-70%) é obstrução por cálculos. (KIMURA *et al.*, 2007) A elevada morbidade e mortalidade associada a ambas entidades torna o manejo da coledocolitíase imperativo e importante foco de estudo e de atualização.

Historicamente, a coledocolitíase era primariamente tratada cirurgicamente. Entretanto, avanços tecnológicos, de imagem, de radiologia intervencionista, endoscópicos, e minimamente invasivos nos últimos 30 anos radicalmente alteraram a avaliação e o manejo de cálculos na via biliar, de modo que a maioria dos casos hoje são resolvidos por especialistas não-cirurgiões. (WILLIAMS *et al.*, 2017)

Do ponto de vista diagnóstico, o estudo inicial de coledocolitíase se baseia em sinais e sintomas, exames laboratoriais séricos e de imagem. Tenta-se estabelecer a probabilidade do diagnóstico bem como do diagnóstico diferencial de outras patologias biliares (colelitíase sintomática, colecistite aguda, etc). Fluxogramas de estratificação de riso podem auxiliar. O mais utilizado, atualizado em 2019, é o da Sociedade Americana de Endoscopia Gastrointestinal (BUXBAUM *et al.*, 2019) sumarizado a seguir[1]:

- Alta probabilidade:
    - evidência de cálculo em ultrassom (US) /imagem transversal ou
    - colangite ou
    - bilirrubina total > 4mg/dL e colédoco dilatado (> 6mm) em US/imagem transversal
- Intermediária probabilidade:
    - Testes de bioquímica hepática alterados ou
    - Idade > 55 anos ou
    - Colédoco dilatado (> 6mm) em US/imagem transversal
- Baixa probabilidade:
    - Ausência dos preditores acima

Diante dessa avaliação, a tomada de decisão no manejo dos pacientes prossegue na tentativa de confirmação do diagnóstico associado ao uso racional de intervenções que sejam efetivas na remoção de cálculos. Pacientes com baixa probabilidade de coledocolitíase são submetidos diretamente à colecistectomia videolaparoscópica, que pode ser acompanhada ou não de colangiografia intraoperatória (CIO) – *ver seção 1.2*. Pacientes com probabilidade intermediária geralmente são submetidos a investigação adicional com modalidades menos invasivas que o eventual tratamento definitivo, seja este cirúrgico (exploração das vias biliares) ou por colangiopancreatografia retrógrada

[1] Simplificado; considera paciente com vesícula biliar tópica, com anatomia gastrointestinal usual.

endoscópica (CPRE). Pacientes com alta probabilidade são encaminhados para tratamento endoscópico por CPRE antes da colecistectomia.

Desde sua introdução, a CPRE foi considerada método padrão-ouro para detecção de cálculos nos ductos biliares além de apresentar a vantagem de possibilitar manejo simultâneo ao diagnóstico. (KAWAI *et al.*, 1974) Entretanto, a CPRE é um método invasivo e operador-dependente associado a complicações, tais como: pancreatite (1,3 a 9,7%), hemorragia (0,3 a 2%), perfuração (0,1 a 1,1%), colangite (0,6 a 5%) e morte (0,1%). Diferentes modalidades de litotripsia podem ser associadas ao procedimento endoscópico em casos de difícil manejo. (DAVEE; GARCIA; BARON, 2012; WILLIAMS *et al.*, 2017) Modernamente métodos menos invasivos são utilizados para diagnóstico, ficando a CPRE indicada principalmente como modalidade terapêutica.

Dentre as mais recentemente desenvolvidas modalidades diagnósticas estão a Colangiopancreatografia por Ressonância Nuclear Magnética (CRNM) e a Ecoendoscopia ou US endoscópico. (GURUSAMY *et al.*, 2015; ROHDE; OSVALDT, 2018) A CRNM, quando comparado ao US transabdominal, representa um estudo não-invasivo que significativamente aumenta sensibilidade (95% vs. 60%) e especificidade (90% vs. 77%) para o diagnóstico de coledocolitíase. (MANDELIA *et al.*, 2013) Ecoendoscopia, exame invasivo, apresenta alta acurácia no diagnóstico de coledocolitíase (97%) e é um importante complemento em casos submetidos à CPRE. (GARROW *et al.*, 2007) Ainda, apresenta maior acurácia quando comparado a CRNM (93% vs. 90%). (DE CASTRO *et al.*, 2016) Entretanto, essas modalidades não se mostraram mais custo-efetivas que CPRE sozinha, no manejo de coledocolitíase em uma série de 163 pacientes dinamarqueses (AINSWORTH *et al.*, 2004). Em estudos de custo-benefício, tanto americano (SONNENBERG *et al.*, 2016) quanto britânico (MORRIS *et al.*, 2015), CNRM parece ser superior à ecoendoscopia em casos com probabilidades pré-teste de coledocolitíase entre 40% e 90% (risco intermediário).

Outra técnica diagnóstica proposta atualmente para visualizar a anatomia das vias biliares é o uso de colangiografia fluorescente infravermelha com verde de indocianina. Apesar de apresentar ótima capacidade para identificação de estruturas anatômicas, com taxas superiores à CIO para esse fim, inclusive em pacientes obesos, a técnica é limitada para detecção de cálculos. (HIWATASHI *et al.*, 2018; PESCE *et al.*, 2015)

A base do tratamento da coledocolitíase é remover os cálculos do colédoco, seja endoscopicamente ou cirurgicamente. O método empregado depende do momento do diagnóstico, da disponibilidade de recursos, e da preferência e *expertise* dos especialistas envolvidos no tratamento desses pacientes.

A exploração cirúrgica das vias biliares deve se dar de forma minimamente invasiva quando factível, especialmente considerando a tendência à tratamento da coledocolitíase em tempo único – ao invés da instauração de procedimentos adicionais no pós-operatório. (GURUSAMY *et al.*, 2015; RICCI *et al.*, 2018; SUN *et al.*, 2016) As duas principais abordagens laparoscópicas são a por via trancística e a por via transcoledociana. Metanálises recentes tem demonstrado que a via transcística é segura e reduz tempo de internação, morbidade e mortalidade quando comparada à procedimento que inclui coledocotomia, mas apresenta menor taxa de remoção completa de cálculos. (BEKHEIT *et al.*, 2019; HAJIBANDEH *et al.*, 2019) Coledocoscopia não é economicamente competitiva com técnicas não cirúrgicas (CPRE) conforme análise em estudo americano (NAGORNEY; LOHMULLER, 1990). Além do custo, existe uma limitação relacionada a falta de cirurgiões com treinamento apropriado e falta de suporte técnico para efetivamente tratar pacientes com patologia biliar complexa. (HELTON; AYLOO, 2019)

A exploração cirúrgica da via biliar por laparotomia, apesar de mais amplamente disponível e menor custo que por via laparoscópica, está associada a mais complicações e maior tempo de internação. (GRUBNIK *et al.*, 2012) A cirurgia aberta ficaria reservada para pacientes onde as modalidades descritas anteriormente falharam, ou não estão facilmente disponíveis. (HELTON; AYLOO, 2019; WILLIAMS *et al.*, 2017) No entanto, é seguro estimar que a maioria dos centros que realizam colecistectomia no mundo – principalmente em países subdesenvolvidos / em desenvolvimento – tem limitada disponibilidade de recursos para tratamento de coledocolitíase.

1.2 COLANGIOGRAFIA INTRAOPERATÓRIA

A colangiografia operatória (CIO) foi descrita por Pablo Mirizzi (MIRIZZI, 1937) e sua utilização em colecistectomias tem sido recomendada desde 1948. A técnica consiste na injeção de substância contrastada na via biliar para captura por exame de imagem. Seu objetivo é, basicamente, prevenir ou identificar lesão de via biliar e detectar a presença de cálculos na via biliar. A CIO é uma importante ferramenta no manejo da coledocolitíase.

Na CIO laparoscópica, genericamente, o procedimento ocorre após a dissecção das estruturas anatômicas necessárias para a realização de uma colecistectomia segura. É feita a clipagem proximal do ducto cístico seguida de uma secção transversa parcial do mesmo. Um cateter, introduzido no abdome por punção, é manipulado pela incisão e é fixado nesta posição. Contraste hidrossolúvel é injetado através do cateter e sua posição é confirmada e ajustada conforme necessário. O cateter é então fixado em sua posição e se inicia a captura do exame de imagem. O exame é realizado de maneira intermitente ou contínua (preferencialmente), visualizado por fluoroscopia.

Em uma colangiografia normal, deve-se conseguir avaliar a extensão do ducto cístico e sua junção com o colédoco, o tamanho e aspecto da via biliar principal; o contraste deve fluir anterogradamente para o duodeno com apenas enchimento discreto dos ductos intra-hepáticos (enchimento vigoroso desse segmento pode sugerir obstrução distal); a anatomia intra- e extra-hepática deve estar dentro da normalidade; defeitos de enchimento não devem estar presentes. (TOWNSEND *et al.*) Defeitos de enchimento correspondem à imagem “flutuante” em relação ao contraste sugestiva de cálculo, ou imagem meniscoide com parada abrupta do contraste – sugestiva de cálculo impactado. (BERCI, 2006) Há ainda descrição de alteração ou de ausência de fluxo de contraste para o duodeno, sem necessariamente identificar-se imagem sugestiva de cálculo. Estudos sugerem que este achado é menos específico, pois poderia significar apenas espasmo do esfíncter de Oddi. Entretanto, não existe diferença no valor preditivo positivo para o diagnóstico de coledocolitíase entre os dois achados descritos. (SINGH *et al.*, 2000; SNOW *et al.*, 2001) A injeção lenta do contraste previne ocorrência de espasmos do esfíncter de Oddi.

Com relação à identificação de cálculos, a CIO apresenta sensibilidade e especificidade na detecção de cálculos que varia entre 75-99% e 90-100%,

respectivamente. (GURUSAMY *et al.*, 2015; VIDEHULT *et al.*, 2009) Apesar da realização da CIO adicionar desprezíveis tempo e recursos adicionais à colecistectomia convencional, existe significativa heterogeneidade em relação ao seu uso. Compara-se extensivamente na literatura a realização de CIO de maneira rotineira, em todos os casos levados à colecistectomia, e a realização em casos selecionados, orientados conforme fluxogramas de estratificação. A maioria dos estudos tem baixo nível de evidência, sem definição que suporte uma ou outra indicação. (FORD *et al.*, 2012; PHOTI *et al.*, 2017). A taxa de sucesso do procedimento é heterogênea: de 80.4-98.9% em centros acadêmicos onde o procedimento é realizado seletivamente, até 66% em centros não acadêmicos, com realização rotineira. (SINGH *et al.*, 2000; SNOW *et al.*, 2001; VIDEHULT *et al.*, 2009)

Ao término da CIO, se retira o cateter e procede-se clipagem do ducto cístico distal à transecção parcial realizada para o estudo colangiográfico. O procedimento cirúrgico prossegue conforme técnica usual.

1.3 MANUTENÇÃO DO CATETER TRANSCÍSTICO NO PÓS-OPERATÓRIO

No manejo do paciente com possível coledocolitíase, após achados sugestivos de cálculos na CIO, a maioria dos centros tem como próximo passo ou a exploração cirúrgica da via biliar ou término do procedimento cirúrgico e encaminhamento do paciente para CPRE pós-operatória. Por vezes, procedimentos endoscópicos não estão disponíveis ou têm períodos de espera indesejáveis ou proibitivos. A exploração das vias biliares depende de tecnologia e treinamento para a modalidade laparoscópica, igualmente impraticável em alguns centros. Resta a modalidade laparotômica que, além de também depender de cirurgião experiente, é muitas vezes indesejada devido à morbidade associada. (COTTON *et al.*, 1991; KAIF *et al.*, 2017; MORRIS *et al.*, 2015; WILLIAMS *et al.*, 2017)

Face a essas considerações, depara-se com a prática particular e pouco descrita na literatura, de manter o cateter colangiográfico na posição transcística (TC) no pós-operatório. (O'DONOVAN *et al.*, 1997). Propõe-se as seguintes racionalizações para justificar essa prática:

I A manutenção do cateter TC possibilita a realização de colangiografias no pós-operatório, potencialmente deferindo intervenções adicionais já que exames subsequentes em paralelo aumentam a sensibilidade e o valor preditivo negativo diagnóstico. Estudos evidenciaram que quase metade dos pacientes com CIO positivas tinham CPREs normais. Inversamente, apenas 48.8% de todas CIOs requereram CPRE no pós-operatório. (COLLINS *et al.*, 2004; ENOCHSSON *et al.*, 2010; GURUSAMY *et al.*, 2015; HORWOOD *et al.*, 2010) Ainda, ambos achados ultrassonográficos de dilatação do colédoco e transaminases persistentemente elevadas tiveram pobre valor preditivo positivo para coledocolitíase. (KAIF *et al.*, 2017)

II O cateter TC serve como dreno e descomprime a via biliar. A pressão aumentada no sistema biliar faz parte da fisiopatologia da dor e da icterícia associadas com coledocolitíase, assim como com o desenvolvimento de pancreatite. Mantendo o cateter poderia ainda, teoricamente, prevenir o aumento da permeabilidade dos dúctulos biliares, não permitindo translocação de bactérias e de toxinas da circulação portal para a via biliar (definidores de colangite).(KIMURA *et al.*, 2007)

III O cateter TC pode auxiliar na CPRE. As CPREs têm uma taxa de falha de 5 a 15% na canulação da papila duodenal usando técnica usual, mesmo por endoscopistas experientes. (LEE *et al.*, 2014) A taxa de sucesso pode ser aumentada para próximo de 98% usando a esfincterotomia "pré-corte". Este é um termo genérico para diferentes técnicas aonde uma incisão na ampola de Vater (ou no colédoco) é feita *antes* de se canular a papila duodenal. (DAVEE; GARCIA; TH., 2012; MAPLE *et al.*, 2010) No entanto, o "pré-corte" é associado com um aumento da taxa de complicações, como pancreatite e perfuração. (DAVEE; GARCIA; BARON, 2012) A manutenção do cateter TC permite que se passe um fio-guia que se exteriorizaria no duodeno. Isso poderia facilitar a canulação da papila pelo endoscópio ou orientar o "pré-corte" durante a CPRE.

Os Serviços de Cirurgia Geral e do Aparelho Digestivo do Hospital de Clínicas de Porto Alegre, RS, Brasil, têm como prática a manutenção do cateter colangiográfico na posição TC para alguns pacientes. Se opta por tal prática como tentativa de suplantar a limitada disponibilidade de CPREs e a dificuldade na realização rotineira de exploração laparoscópica das vias biliares no contexto do Sistema Único de Saúde (SUS). Além disso, propõe-se que a prática reduziria o número de explorações cirúrgicas das vias biliares por via laparotômica.

1.4 REFERÊNCIAS

AINSWORTH, A. P.; RAFAELSEN, S. R.; WAMBERG, P. A.; PLESS, T. *et al.* Cost-effectiveness of endoscopic ultrasonography, magnetic resonance cholangiopancreatography and endoscopic retrograde cholangiopancreatography in patients suspected of pancreaticobiliary disease. **Scand J Gastroenterol**, 39, n. 6, p. 579-583, Jun 2004.

BEKHEIT, M.; SMITH, R.; RAMSAY, G.; SOGGIU, F. *et al.* Meta-analysis of laparoscopic transcystic versus transcholedochal common bile duct exploration for choledocholithiasis. **BJS Open**, 3, n. 3, p. 242-251, Jun 2019.

BERCI, G. Laparoscopic Cholecystectomy: Cholangiography. *In*: SCOTT-CONNER, C. E. H. (Ed.). **The SAGES Manual: Fundamentals of Laparoscopy, Thoracoscopy, and GI Endoscopy**. New York, NY: Springer New York, 2006. p. 145-164.

BUXBAUM, J. L.; ABBAS FEHMI, S. M.; SULTAN, S.; FISHMAN, D. S. *et al.* ASGE guideline on the role of endoscopy in the evaluation and management of choledocholithiasis. **Gastrointestinal Endoscopy**, 89, n. 6, p. 1075-1105.e1015, 2019.

CHEN, H.; JORISSEN, R.; WALCOTT, J.; NIKFARJAM, M. Incidence and predictors of common bile duct stones in patients with acute cholecystitis: a systematic literature review and meta-analysis. **ANZ J Surg**, Nov 19 2019.

COELHO, J. C.; BONILHA, R.; PITAKI, S. A.; CORDEIRO, R. M. *et al.* Prevalence of gallstones in a Brazilian population. **Int Surg**, 84, n. 1, p. 25-28, Jan-Mar 1999.

COLLINS, C.; MAGUIRE, D.; IRELAND, A.; FITZGERALD, E. *et al.* A prospective study of common bile duct calculi in patients undergoing laparoscopic cholecystectomy: natural history of choledocholithiasis revisited. **Ann Surg**, 239, n. 1, p. 28-33, Jan 2004.

COTTON, P. B.; LEHMAN, G.; VENNES, J.; GEENEN, J. E. *et al.* Endoscopic sphincterotomy complications and their management: an attempt at consensus. **Gastrointest Endosc**, 37, n. 3, p. 383-393, May-Jun 1991.

DASARI, B. V.; TAN, C. J.; GURUSAMY, K. S.; MARTIN, D. J. *et al.* Surgical versus endoscopic treatment of bile duct stones. **Cochrane Database Syst Rev**, n. 12, p. CD003327, Dec 12 2013.

DAVEE, T.; GARCIA, J.; TH., B. Precut sphincterotomy for selective biliary duct cannulation during endoscopic retrograde cholangiopancreatography. **Annals of Gastroenterology**, n. 25, p. 291-302, 2012.

DAVEE, T.; GARCIA, J. A.; BARON, T. H. Precut sphincterotomy for selective biliary duct cannulation during endoscopic retrograde cholangiopancreatography. **Ann Gastroenterol**, 25, n. 4, p. 291-302, 2012.

DE CASTRO, V. L.; MOURA, E. G.; CHAVES, D. M.; BERNARDO, W. M. *et al.* Endoscopic ultrasound versus magnetic resonance cholangiopancreatography in suspected choledocholithiasis: A systematic review. **Endosc Ultrasound**, 5, n. 2, p. 118-128, Mar-Apr 2016.

ENOCHSSON, L.; SWAHN, F.; ARNELO, U.; NILSSON, M. *et al.* Nationwide, population-based data from 11,074 ERCP procedures from the Swedish Registry for Gallstone Surgery and ERCP. **Gastrointest Endosc**, 72, n. 6, p. 1175-1184, 1184.e1171-1173, Dec 2010.

EVERHART, J. E.; KHARE, M.; HILL, M.; MAURER, K. R. Prevalence and ethnic differences in gallbladder disease in the United States. **Gastroenterology**, 117, n. 3, p. 632-639, Sep 1999.

FESTI, D.; REGGIANI, M. L.; ATTILI, A. F.; LORIA, P. *et al.* Natural history of gallstone disease: Expectant management or active treatment? Results from a population-based cohort study. **J Gastroenterol Hepatol**, 25, n. 4, p. 719-724, Apr 2010.

FORD, J. A.; SOOP, M.; DU, J.; LOVEDAY, B. P. *et al.* Systematic review of intraoperative cholangiography in cholecystectomy. **Br J Surg**, 99, n. 2, p. 160-167, Feb 2012.

GARROW, D.; MILLER, S.; SINHA, D.; CONWAY, J. *et al.* Endoscopic ultrasound: a meta-analysis of test performance in suspected biliary obstruction. **Clin Gastroenterol Hepatol**, 5, n. 5, p. 616-623, May 2007.

GRUBNIK, V. V.; TKACHENKO, A. I.; ILYASHENKO, V. V.; VOROTYNTSEVA, K. O. Laparoscopic common bile duct exploration versus open surgery: comparative prospective randomized trial. **Surg Endosc**, 26, n. 8, p. 2165-2171, Aug 2012.

GURUSAMY, K. S.; GILJACA, V.; TAKWOINGI, Y.; HIGGIE, D. *et al.* Endoscopic retrograde cholangiopancreatography versus intraoperative cholangiography for diagnosis of common bile duct stones. **Cochrane Database Syst Rev**, n. 2, p. Cd010339, Feb 26 2015.

HAJIBANDEH, S.; HAJIBANDEH, S.; SARMA, D. R.; BALAKRISHNAN, S. *et al.* Laparoscopic Transcystic Versus Transductal Common Bile Duct Exploration: A Systematic Review and Meta-analysis. **World J Surg**, 43, n. 8, p. 1935-1948, Aug 2019.

HELTON, W. S.; AYLOO, S. Technical Aspects of Bile Duct Evaluation and Exploration: An Update. **Surg Clin North Am**, 99, n. 2, p. 259-282, Apr 2019.

HIWATASHI, K.; OKUMURA, H.; SETOYAMA, T.; ANDO, K. *et al.* Evaluation of laparoscopic cholecystectomy using indocyanine green cholangiography including cholecystitis: A retrospective study. **Medicine (Baltimore)**, 97, n. 30, p. e11654, Jul 2018.

HORWOOD, J.; AKBAR, F.; DAVIS, K.; MORGAN, R. Prospective evaluation of a selective approach to cholangiography for suspected common bile duct stones. **Ann R Coll Surg Engl**, 92, n. 3, p. 206-210, Apr 2010.

KAIF, M.; AGRAWAL, D.; SREENARASIMHAIAH, J. Can clinical factors predict the need for intervention after a positive intraoperative cholangiogram? **J Dig Dis**, 18, n. 7, p. 410-415, Jul 2017.

KAWAI, K.; AKASAKA, Y.; MURAKAMI, K.; TADA, M. *et al.* Endoscopic sphincterotomy of the ampulla of Vater. **Gastrointest Endosc**, 20, n. 4, p. 148-151, May 1974.

KIMURA, Y.; TAKADA, T.; KAWARADA, Y.; NIMURA, Y. *et al.* Definitions, pathophysiology, and epidemiology of acute cholangitis and cholecystitis: Tokyo Guidelines. **J Hepatobiliary Pancreat Surg**, 14, n. 1, p. 15-26, 2007.

KO, C. W.; LEE, S. P. Epidemiology and natural history of common bile duct stones and prediction of disease. **Gastrointest Endosc**, 56, n. 6 Suppl, p. S165-169, Dec 2002.

LEE, T. H.; HWANG, S. O.; CHOI, H. J.; JUNG, Y. *et al.* Sequential algorithm analysis to facilitate selective biliary access for difficult biliary cannulation in ERCP: a prospective clinical study. **BMC Gastroenterol**, 14, p. 30, 2014.

LIU, C. L.; LO, C. M.; FAN, S. T. Acute biliary pancreatitis: diagnosis and management. **World J Surg**, 21, n. 2, p. 149-154, Feb 1997.

MANDELIA, A.; GUPTA, A. K.; VERMA, D. K.; SHARMA, S. The Value of Magnetic Resonance Cholangio-Pancreatography (MRCP) in the Detection of Choledocholithiasis. **J Clin Diagn Res**, 7, n. 9, p. 1941-1945, Sep 2013.

MANNING, A.; FRAZEE, R.; ABERNATHY, S.; ISBELL, C. *et al.* Protocol-Driven Management of Suspected Common Duct Stones. **J Am Coll Surg**, 224, n. 4, p. 645-649, Apr 2017.

MANTOVANI, M.; LEAL, R. F.; FONTELLES, M. J. Incidência de colelitíase em necropsias realizadas em hospital universitário no município de Campinas-SP. **Revista do Colégio Brasileiro de Cirurgiões**, 28, p. 259-263, 2001.

MAPLE, J. T.; BEN-MENACHEM, T.; ANDERSON, M. A.; APPALANENI, V. *et al.* The role of endoscopy in the evaluation of suspected choledocholithiasis. **Gastrointest Endosc**, 71, n. 1, p. 1-9, Jan 2010.

MIRIZZI, P. L. Operative Cholangiography. **Surg Gynec Obstet**, 65, n. Nov, p. 702-710, 1937.

MOORE, K. L.; AGUR, A. M. R.; DALLEY, A. F. **Clinically oriented anatomy**. 2019. 9781975150860 1975150864.

MORRIS, S.; GURUSAMY, K. S.; SHERINGHAM, J.; DAVIDSON, B. R. Cost-effectiveness analysis of endoscopic ultrasound versus magnetic resonance cholangiopancreatography in patients with suspected common bile duct stones. **PLoS One**, 10, n. 3, p. e0121699, 2015.

NAGORNEY, D. M.; LOHMULLER, J. L. Choledochoscopy. A cost-minimization analysis. **Ann Surg**, 211, n. 3, p. 354-359, Mar 1990.

O'DONOVAN, A. N.; O'SULLIVAN, G.; IRELAND, A.; FITZGERALD, E. Prospective trial of the role of fine bore intubation of the cystic duct at the time of operative cholangiography. **J Am Coll Surg**, 184, n. 3, p. 262-264, Mar 1997.

PESCE, A.; PICCOLO, G.; LA GRECA, G.; PULEO, S. Utility of fluorescent cholangiography during laparoscopic cholecystectomy: A systematic review. **World J Gastroenterol**, 21, n. 25, p. 7877-7883, Jul 7 2015.

PHOTI, E. S.; EL-HADI, A.; BROWN, S.; SWAFE, L. *et al.* The Routine Use of Cholangiography for Laparoscopic Cholecystectomy in the Modern Era. **JSLS**, 21, n. 3, Jul-Sep 2017.

PORTINCASA, P.; MOSCHETTA, A.; PALASCIANO, G. Cholesterol gallstone disease. **Lancet**, 368, n. 9531, p. 230-239, Jul 15 2006.

RICCI, C.; PAGANO, N.; TAFFURELLI, G.; PACILIO, C. A. *et al.* Comparison of Efficacy and Safety of 4 Combinations of Laparoscopic and Intraoperative Techniques for Management of Gallstone Disease With Biliary Duct Calculi: A Systematic Review and Network Meta-analysis. **JAMA Surg**, 153, n. 7, p. e181167, Jul 18 2018.

ROHDE, L.; OSVALDT, A. B. **Rotinas em Cirurgia Digestiva**. 3a ed. Porto Alegre RS: 2018.

SHABANZADEH, D. M.; SØRENSEN, L. T.; JØRGENSEN, T. A Prediction Rule for Risk Stratification of Incidentally Discovered Gallstones: Results From a Large Cohort Study. **Gastroenterology**, 150, n. 1, p. 156-167.e151, Jan 2016.

SINGH, G.; GUPTA, P. C.; SRIDAR, G.; KATARIYA, R. N. Role of selective intra-operative cholangiography during cholecystectomy. **Aust N Z J Surg**, 70, n. 2, p. 106-109, Feb 2000.

SNOW, L. L.; WEINSTEIN, L. S.; HANNON, J. K.; LANE, D. R. Evaluation of operative cholangiography in 2043 patients undergoing laparoscopic cholecystectomy: a case for the selective operative cholangiogram. **Surg Endosc**, 15, n. 1, p. 14-20, Jan 2001.

SONNENBERG, A.; ENESTVEDT, B. K.; BAKIS, G. Management of Suspected Choledocholithiasis: A Decision Analysis for Choosing the Optimal Imaging Modality. **Dig Dis Sci**, 61, n. 2, p. 603-609, Feb 2016.

STINTON, L. M.; SHAFFER, E. A. Epidemiology of gallbladder disease: cholelithiasis and cancer. **Gut Liver**, 6, n. 2, p. 172-187, Apr 2012.

SUN, S. X.; KULAYLAT, A. N.; HOLLENBEAK, C. S.; SOYBEL, D. I. Cost-effective Decisions in Detecting Silent Common Bile Duct Gallstones During Laparoscopic Cholecystectomy. **Ann Surg**, 263, n. 6, p. 1164-1172, Jun 2016.

TORRES, O. J. M.; BARBOSA, É. S.; PANTOJA, P. B.; DINIZ, M. C. S. *et al.* Prevalência ultra-sonográfica de litíase biliar em pacientes ambulatoriais. **Revista do Colégio Brasileiro de Cirurgiões**, 32, p. 47-49, 2005.

TOWNSEND, C. R.; BEAUCHAMP, D. B.; KENNETH, M. E.; (EDS.). **Sabiston textbook of surgery: the biological basis of modern surgical practice**. 20th ed. Philadelphia, PA: Elsevier, 3rd June 2016.

VIDEHULT, P.; SANDBLOM, G.; RASMUSSEN, I. C. How reliable is intraoperative cholangiography as a method for detecting common bile duct stones? : A prospective population-based study on 1171 patients. **Surg Endosc**, 23, n. 2, p. 304-312, Feb 2009.

WILLIAMS, E.; BECKINGHAM, I.; EL SAYED, G.; GURUSAMY, K. *et al.* Updated guideline on the management of common bile duct stones (CBDS). **Gut**, 66, n. 5, p. 765-782, May 2017.

2 OBJETIVOS

2.1 Objetivo Geral

Comparar a taxa de complicações entre pacientes submetidos a colecistectomia videolaparoscópica com colangiografia intraoperatória com achados positivos que tiveram mantido cateter na posição trancística no pós-operatório com aqueles em que o cateter não fora mantido.

2.2 Objetivos Específicos

I Estimar o risco de complicações associadas à manutenção de cateter TC no pós-operatório comparativamente a não o manter.

II Verificar redução no número de CPREs e outros recursos diagnósticos e terapêuticos no manejo da coledocolitíase utilizando prática de manutenção de cateter TC no pós-operatório.

3 ARTIGO PARA SUBMISSÃO

Original Article

Intraoperative Cholangiography with Filling Defects: Comparative Analysis of Complications of Postoperative Transcystic Duct (TCD) Catheter Maintenance

"Transcystic duct catheter maintenance complications"

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ABSTRACT

Background: This is a *retrospective cohort* of patients undergoing laparoscopic cholecystectomy with intraoperative cholangiography (IOC) with positive findings for filling defects. A comparative assessment in complication rates was performed for patients that had their cholangiography catheter maintained in its transcystic duct (TCD) position postoperatively. This is a practice proposed to overcome the limited availability of Endoscopic Retrograde Cholangiopancreatography (ERCP) as well as to avoid surgical exploration of the common bile duct.

Methods: A retrospective medical record review of all positive IOC from January 2015 to December 2018 was performed. Patients' demographic and perioperative data from the hospital stay period in which the cholecystectomy occurred until the last surgical ambulatory visit was compared between groups (with vs. without TCD catheter). Complications were operationalized using the Clavien-Dindo scale.

Results: Univariate analysis of complications showed a 2.4-fold risk increase in complications (95% CI 1.13 to 5.1) between comparison groups. Number of ERCPs (18 vs. 30 were not significantly different between maintaining or not the TCD catheter postop, respectively. Stratified analysis followed by exact logistic regression supported the findings that maintaining the TCD catheter postoperatively increased complication rates (OR=5.34, 95% CI 1.22, 29.83, p=0.022), adjusting for potential confounders.

Conclusion: The maintenance of the TCD catheter postoperatively did not prove to be effective in significantly reducing the number of ERCP nor associated complications. Also, outcomes inherited from the practice caused adverse events that surpassed its potential benefits. Moreover, expectant follow-up is reasonable for patients with evidence of common bile duct stones, even in setting with limited resource availability. We do not recommend this practice, even in settings where there are limited resources of more modern management of choledocholithiasis.

Key Words: Choledocholithiasis, cholangiography, transcystic duct catheter, complications

INTRODUCTION

Choledocholithiasis is estimated to be present at the moment of a patient's cholecystectomy in 5-20 percent of cases.[1-3] Considering the prevalence of symptomatic gallbladder lithiasic disease, the presence of common bile duct (CBD) stones is a relevant condition that predisposes patients to potentially lethal conditions such as pancreatitis and cholangitis. [1, 2, 4]

Modern diagnostic and therapeutic modalities such as Magnetic Resonance cholangiopancreatography (MRCP), Endoscopic Ultrasound (EUS), Endoscopic retrograde cholangiopancreatography (ERCP), and diverse types of lithotripsy are effective in managing CBD stones, with a trend towards single-stage approaches. [2, 5, 6] In most institutions worldwide, however, these procedures are impractical as they occur at limited availability. Another diagnostic tool is indocyanine green fluorescent cholangiography that identifies the biliary tree during surgery, but is limited in detecting CBD stones[7].

Intraoperative cholangiography (IOC) remains an important tool in the management of choledocholithiasis. The reported sensitivity and specificity of IOC in the detection of stones range between 75–99% and 90–100%, respectively.[2, 8] There is extensive analysis on the selective vs. routinely performance of IOC, and not enough robust evidence to support or abandon its current use [9, 10]. This study, however, focuses on a particular practice: the maintenance of the cholangiography catheter in its transcystic duct position postoperatively upon findings of filling defects in the IOC[11].

Common bile duct surgical exploration or postoperative ERCP is the usual next step after a positive finding in the IOC. They both present partial availability in many settings and potential complications.[12-15] Considering that, the rationale behind the maintenance of the transcystic duct (TCD) catheter is that:

1. It warrants the possibility of performing postoperative cholangiography, potentially deferring additional interventions: Studies have found normal ERCP in nearly half of patients with a positive IOC.[2, 16-18] Also, only 48.8% of all positive IOC studies required a therapeutic ERCP. Furthermore, both sonographic findings of bile duct dilation and persistent transaminase elevations had poor positive predictive value for choledocholithiasis.[14]

2. It decompresses the biliary tract: Arguably, pressure within the biliary system is part of the pathophysiology of pain and jaundice associated with choledocholithiasis, as well as with the

onset of pancreatitis. Maintaining the catheter would also, theoretically, prevent increased permeability of bile ductuli, not allowing translocation of bacteria and toxins from the portal circulation into the biliary tract, which defines cholangitis.[4]

3. It may aid ERCP: ERCP has a failure rate ranging from 5% to 15%, even in experienced hands[19] using standard techniques. Success rate can be increased by up to 98% using precut sphincterotomy, a generic term for different techniques where an incision into the ampulla of Vater or CBD is made *prior* to biliary cannulation.[20, 21] However, precut sphincterotomy is associated with a reported increase in complication rates, such as pancreatitis and perforation.[22] The maintenance of the TCD catheter might allow anterograde guide wiring that exteriorizes in the papilla which could facilitate cannulation or assist the precut during ERCP.

There is but one group[11, 18] that studied this practice of maintaining the cholangiography catheter postoperatively in the literature. We evaluated this practice for complications in a comparative analysis.

METHODS

Over a 4-year period (January 2015 to December 2018), 2564 patients underwent laparoscopic cholecystectomy within Brazil's universal health system (SUS) at the Hospital de Clinicas de Porto Alegre, RS-Brazil. Surgery residents performed most of the procedures (94%) under attending staff supervision. Five hundred eighty-five of these patients (22.82%) had IOC performed successfully during cholecystectomy. These patients had their surgical notes evaluated for the description of filling defects during IOC. It was considered filling defects both "floating" defects within the contrasted bile duct during cholangiography, and non-passage or delayed passage of contrast to the duodenum despite manipulation and/or hyoscine IV administration. Eighty-four patients (3.27%) met criteria for filling defects and were included in the study. One patient had their cholangiography performed through the gallbladder and underwent partial cholecystectomy and was excluded. *The remaining 83 patients represent the retrospective cohort evaluated.*

Intraoperative cholangiography (IOC) was performed using a 16Ga subclavian "intracath" catheter with a needle protector (BIOCAT, Biomedical®). This was introduced through the abdominal wall via a needle through a separate skin puncture wound and advanced through the

cystic duct. Warm saline was instilled through the catheter while it was secured with one titanium clip (Ligaclip®Extra, Ethicon) until mild resistance arose, and no leakage was observed. Two syringes (one containing saline and the other contrast– 30% Hypaque solution) were connected to the system using a 3-way stopcock. Bile was aspirated through the connecting system to eliminate gas bubbles. After satisfactory connection, 3-5 mL of contrast was injected, and the biliary tree was imaged using a c-arm radiograph. Further contrast was injected, and the operating table position was altered as needed. At least two films were obtained and interpreted by the surgeon attending and resident(s) at the time of the procedure. In cases of delayed passage of contrast to the duodenum, the anesthesiologist administered hyoscine intravenously, and cholangiography was repeated. At this point, the attending surgeon supervising the case decided whether to maintain the catheter in situ and add a second clip to secure it or to remove the catheter and double clip the cystic duct. After these procedures, the cholecystectomy was completed laparoscopically as usual. No change in equipment or materials occurred during the evaluation period.

We reviewed patients' medical records from the admission date of the hospital period in which the cholecystectomy was performed until the last general surgery ambulatory visit. Data on demographics, comorbidities, and surgical parameters as well as preoperative signs, symptoms, laboratory exams, and diagnosis were recorded. Preoperative laboratories represent the last exam prior to surgery. The decision to perform IOC (whether pre- or intraoperatively) was reviewed from surgical notes and preoperatory evaluations. Cystic duct manipulation refers to performing saline flushes, using intravenous hyoscine, and/or using catheters (e.g., Fogarty) to attempt duct clearing. None of the attending surgeons in our department performs IOC routinely, but in 10 positive IOC cases (12%), the information was not explicitly found, and it was coded as "not justified". Patients records were evaluated for subsequent management with imaging, endoscopic, or new surgical interventions.

Complication rate was the primary outcome and was classified according to the Clavien-Dindo classification[23] as minor (grade II) or major (grade III or higher). Catheter dislocation perceived during the hospital stay (either in postoperative cholangiography, ERCP, or pulled) that did not require invasive procedures were included in the minor complication category despite being Clavien-Dindo grade I. Patients with drain dislocation that required reoperation (Clavien-Dindo grade IIIb) were included in the major category. Proportion of postoperative ERCPs and MRCPs performed, as well as length of hospital stay after cholecystectomy, and

number of laboratory exams ordered, were assessed as secondary outcomes.

Statistical analysis was conducted using SAS software, version 9.4 (SAS Institute). Differences between means were tested with the Student t-test, and proportions were compared with the x^2 statistic as well as their non-parametrical counterparts. A p-value of less than 0.05 was deemed significant. Cochran-Mantel-Haenszel adjusted estimates were used in stratified analysis of complications before multivariable model fitting due to the small number of complications in our data. An exact logistic regression analysis was used to account for cofactors in the complication rates among groups due to sparse data. The study was conducted in accordance with the ethical guidelines of our Institution under IRB approval number 2.953.930.

RESULTS

General Cohort and Comparative Groups

Twenty-eight patients (33.73%) had the TCD catheter maintained in situ postoperatively, while 55 patients (66.27%) had the TCD catheter removed before having their cholecystectomy completed (comparative group). Most subjects were women (74.7%) aged 48.5±19 years and had at least one comorbidity (69.9%). Between 17 and 28% of the cohort presented with clinical signs of cholestasis (jaundice, choluria, or pale stools), and 26.5% had imaging showing a CBD larger than 6mm preoperatively[20, 24]. The TCD catheter group was on average older (49.08±17.36 vs. 48.37±19.41 years), had overall fewer comorbidities (82.1% vs. 63.6%), and showed lower values for laboratory findings when compared to their counterpart without statistical significance (Table 1). They were statistically significantly more likely to be diabetic (35.7% vs. 3.6%, Fisher's exact $p<0.001$). All demographic and preoperative characteristics can be found in Table 1.

Operative Characteristics

Cholecystectomies durations had a median of 135 minutes (ranging from 60 to 360 minutes) with a non-significant difference of 137.5 min vs. 130 min between the TCD catheter group and the comparison group, respectively ($Z=0.145$, $p=0.885$). Forty-nine (59%) of the procedures were classified as urgent, with no difference in the between-group comparison (57.1% vs. 60%, $X^2_{(1)}=0.063$, $p=0.802$). Among the preoperative diagnosis, CBD stones (28.9%) and biliary pancreatitis (28.9%) were the most prevalent, followed by acute cholecystitis (21.7%), and symptomatic cholelithiasis (20.5%). There was no significant

difference in proportions of preoperative diagnosis between groups ($X^2_{(3)}$=4.475, p=0.215). The TCD catheter maintenance group of patients presented greater proportion of cases of acute cholecystitis (32.1% vs. 16.4%, $X^2_{(1)}$=2.720, p=0.099), and lower proportion of CBD exploration (3.6% vs. 20%, Fisher's exact p=0.0522), intraoperative complications (0% vs. 5.5%, Fisher's exact p=0.548), and conversion to open surgery (0% vs. 3.6%, Fisher's exact p=0.548) when compared to patients where the catheter was removed after IOC, without statistical significance. All intraoperative complications were resolved laparoscopically. The two conversions to open surgery (2.41%) occurred in the comparative and resulted in CBD explorations. The majority of the reasoning to perform the IOC was done preoperatively (83.1%), mostly due to preoperative ultrasound (US) or MRCP or ERCP findings (33.7%) or due to previous pancreatitis (24.1%). Both IOC moment of decision and indication reasoning variables showed no statistically different proportion between comparison groups (Fisher's exact p=0.764 and p=0.590, respectively). The TCD catheter group had a statistically significant difference in proportion of drains left postoperatively compared to the group where the TCD catheter was removed, with more Penrose drains left (75% vs. 20%), and less Kehr drains (3.57% vs. 12.73%) or no drains (21.43% vs. 67.27%) (Fisher's exact p<.0001). Both conversion to open surgery (Fisher's exact p=0.02) and drains left (Fisher's exact p<.0001) were associated with CBD exploration and with each other (Fisher's exact p=0.008).

Common bile duct exploration was performed in 12 patients (14.5%), two via cystic duct (in one a TCD catheter was maintained), one through a gallbladder infundibulum-CBD fistula, and 9 with choledochotomy. Among the latter, two were converted to open surgery, one exploration used a choledochoscope, and the other used a pediatric fibrobronchoscope. In one case, a Kehr drain was not left within the CBD.

Operative characteristics are summarized in Table 2.

Complications and Postoperative Characteristics

The postoperative complication rate in the present cohort was 20/83 (24.1%), with 17 (20.5%) minor and 3 (3.6%) major complications. When analyzed between the comparison groups, the variable rendered a non-significant difference in proportions (Fisher's exact p=0.06). Then, complication occurrence was analyzed in a binary fashion (i.e., Clavien-Dindo ≥ Grade II), and the group where the TCD catheter was left in situ postoperatively presented statistically more complications (39.3% vs. 16.4%, $X^2_{(1)}$=5.33, p=0.021). At a 5% significance level, the risk of complications in patients where the TCD catheter was maintained postoperatively was 2.4

(95%CI 1.13 – 5.11) times the risk of those where it was removed after IOC. We conducted further stratified and multivariable analyses on complications in the comparison groups with different predictors – see session '*Complications*'.

The median catheter maintenance time, between the cholecystectomy and removal, was 35 days (range 4 – 87). Fifteen patients of the 28 that maintained the TCD catheter underwent postoperative cholangiography. The median time to undergo the first cholangiography through the drain was 4 days (range from 1 to 30 days). Three patients (20%) showed the catheter off the TCD position, 9 (60%) showed sustained filling defects and underwent additional interventions, and 3 (20%) were normal, not requiring additional interventions.

Forty-eight (57.8%) and twenty-two (26.5%) patients underwent ERCP and MRCP after the cholecystectomy, respectively. The proportion of ERCPs performed postoperatively in the TCD catheter group was 64.3% compared to 54.5% in the comparison group ($X^2_{(1)}$=0.722, p=0.396). The proportion of MRCPs performed postoperatively in the TCD catheter group was 17.9% compared to 30.9% in the comparison group ($X^2_{(1)}$=1.623, p=0.203). The median days of hospital stay in our cohort were 10 (range 2-43 days), with a median of 12 days for the TCD catheter group vs. 10 for the comparison group (Z=0.362, p=0.717). The number of laboratories ordered postoperatively during hospital stay had a median of 22 labs (range 0-99) with a non-statistical difference between the TCD catheter and the comparison group (20 vs. 22 days, respectively, Z=-1.290, p=0.197).

Postoperative characteristics are displayed in Table 3.

Complications

Considering the major complications that occurred in our cohort, two were due to bile peritoneum after dislocation of the TCD catheter requiring reoperation, and the third was one patient that presented with septic shock after CBD exploration (no TCD catheter maintained postoperatively). Minor complications were 6 drain dislocations not requiring invasive interventions (3 perceived during ERCP, two during postoperative cholangiography, and one pulled out by the patient), 5 post-ERCP pancreatitis (two in the TCD catheter group and 3 in the comparison group), 3 post-CBD exploration biliary-cutaneous fistulas (all in the comparison group), two pulmonary infections (one in each group), and one bradycardia (in the comparison group).

Looking at the stratified analysis of complications for our comparison groups by different predictors (Table 4), the result of the Cochran-Mantel-Haenszel was significant for several variables. This suggests that the increased risk of having complications amongst patients who maintained the TCD catheter is still statistically significant even after adjusting for those variables. The adjusted risk ratio (RR_A) for having at least one comorbidity (RR_A=2.03, 95%CI 0.98-4.21), diabetes (RR_A=1.71, 95%CI 0.91-4.21), AST increased 3-times the reference value (RR_A=1.88, 95%CI 0.88-4), altered alkaline phosphatase (RR_A=1.57, 95%CI 0.65-3.8), and drains maintained in the post-operative (RR_A=1.46, 95%CI 0.68-3.14) were not statistically significant. These findings suggest potential complete confounding of the relationship between TCD catheter maintenance and complication events. A decision was made not to include all of them in the preliminary logistic model due to collinearity: Diabetes was associated to having any comorbidity (Fisher's exact p<.001), both AST and alkaline phosphatase were associated with preoperative diagnosis (Fisher's exact p=0.002), and drains were associated with the maintenance of the TCD catheter (Fisher's exact p<0.001).

Some variables have appreciably different estimates among strata indicating modification of the effect of TCD catheter maintenance on complication rates: Fifty-year or older patients, hypertensive, diabetic, obese, with normal CBD diameter in a preoperative ultrasound, AST no greater than 3-times the reference value, elective cholecystectomy, preoperative decision to perform IOC, IOC indication due to reasons other than trans operative anatomy, cystic duct manipulation, leaving a Penrose, and not undergoing ERCP post-operatively seems to reduce the magnitude of the crude estimate. This can be seen in Table 4, comparing RRs among strata for each predictor variable. Of notice, IOC decision moment and IOC reasoning were associated with pre-operative diagnosis (Fisher's exact p=0.0091 and Fisher's exact p<0.0001, respectively).

An exact logistic regression was performed to ascertain the effect of maintaining the TCD catheter postoperatively on the likelihood of complication occurrence, adjusted for age, having at least one comorbidity, preoperative diagnosis, intraoperative complications, and CBD exploration (Table 5). The regression model was statistically significant, $X^2(8) = 28.099$, p = 0.0005. The model correctly classified 85.5% of cases. Patients in which the TCD catheter was maintained postoperatively were 5.34 times (95% CI 1.22, 29.83, p=0.022) more likely to present complications than those in which the catheter was not maintained, accounting for all other variables in the model. A one-year increase in age (OR=1.04, 95% CI 1.01, 1.08, p=0.030)

and having at least one comorbidity (OR=5.62, 95% CI 1.31, 55.87, p=0.025) were associated with an adjusted increase likelihood of presenting complications. There is a significant association between the preoperative diagnosis and complication occurrence, after accounting for the other variables in the model (Score test statistic = 7.76, p=0.048). Having a preoperative diagnosis of post biliary pancreatitis was significantly associated with a decrease in the likelihood of presenting postoperative complications when compared to symptomatic gallstone accounting for all other variables in the model (OR=0.05, 95%CI <0.01, 0.69, p=0.002).

DISCUSSION

Complications. In this retrospective cohort, maintaining the cholangiography catheter in its transcystic position upon the finding of filling defects was associated with an over 5-fold increase in complications when compared to standard procedure, adjusted for potential confounders. The model constructed accounted for the effect of postoperative ERCPs performed, whether they were avoided or not and its associated complications (namely, post-ERCP pancreatitis). Still, the hypothesized benefits of this practice seem to have been outweighed by its risks. We consider some rationale for this result when compared to previous data[11, 18] on this practice. In our institution, cholecystectomies were performed by surgical residents, in variable levels of training, and different attendings as oppose to a single surgeon. That contributes to both greater variability in result findings and complication rates. Another aspect that potentially contributed to this difference is cohorts' characteristics due to health systems and socioeconomic structures that differ between countries. The catheter maintained in the TCD position in this study is different compared to the one used by Collins et al.[18] They used a ureteral catheter as oppose to an intravascular one, which might have contributed to greater dislocations in our cohort (8/28). Tract formation relies on a foreign-body reaction consisting of acute and chronic inflammatory processes, which occurs less for the smooth polyurethane surface of vascular catheters than for other biomaterials.[25] Catheter dislocation directly contributed to complication occurrence. Moreover, lack of standardization in the care of CBD stones in our institution in regard to postoperative cholangiograms through the TCD catheter might have reduced its potential protective effects and represent a limitation to our results.

In our setting, cholecystectomy cases with positive IOCs after biliary pancreatitis significantly

rendered fewer complication occurrences compared to symptomatic cholelithiasis when adjusted for all other variables in the model. The same occurred for patients with a pre-cholecystectomy diagnosis of acute cholecystitis and choledocholithiasis, without achieving statistical significance. We hypothesize that this reduction, particularly for post-pancreatitis patients, is due to the fact that many of these patients have already had their main biliary duct cleared, as opposed to occult CBD stones diagnosed in cases previously thought to be symptomatic cholelithiasis. The latter cases are more likely to experience the array of further investigation and interventions accountable for potential complications. Assuming a lower prevalence of CBD stones in this subset of patients, postoperative cholangiography through the TCD catheter would have a smaller positive predictive value. The theoretical increase in benefit to harm ratio of maintaining the catheter postoperatively by reducing unnecessary ERCPs and CBD explorations as initially proposed do not seem to hold in our data. In light of our finding, the potential benefit of maintaining the catheter postoperatively in cases post biliary pancreatitis to confirm results false-positive IOCs is even less warranted.

In our study, predictors of common bile duct stones[20] such as AST and alkaline phosphatase potentially confounded the estimation of complications in our comparison groups towards weaker associations. Patients with altered marker values presented a higher risk for complications associated with the TCD catheter maintenance when compared to patients without altered markers (OR = 6.86 vs. 1.35 for AST, and OR = 1.9 vs. 1.36 for alkaline phosphatase). This result is likely related to these laboratories suggesting that the patient was submitted to cholecystectomy with CBD stones, either in an acute setting or because ERCP was not available. In both cases, we would expect increased complication rates. Cases where the patient was not expected to undergo IOC in the preoperative planning phase and those that underwent IOC due to intraoperative anatomy uncertainty had a higher risk of complications of their respective strata (RR=5, 95%CI 1.45-17.27, and RR=4, 95% CI 1.12-13.29). Those were cases more likely to be more complex, with greater operative times, with more CBD manipulation, and more likely to have occurred during acute cholecystitis, which can explain these results. These characteristics, however, did not appreciably change the risk of complications. The effect of preoperative diagnosis was separated from the effect of the TCD catheter through regression.

General Cohort and Comparative Groups. Despite the presence of complications that differs our cohort from that of Collins et al.[18], we had similar proportions conversion rates (2.4% vs. 2.1%) and intraoperative complications (3 vs. none). Our cohort presented a similar overall

demographic profile of gender (75% vs. 80% of women) and age (48 ±19 vs. 49 ±15 years), expected for biliary disease populations. Acute presentations represented 11% of cholecystectomies cases in their cohort compared to 21% in ours, which can be attributed to our sample of only cholecystectomies with positive IOCs[24]. Our model did predict a significant adjusted increase in complications for patients with at least one comorbidity and who were older. However, intraoperative complications were not significant for the same relationship, probably due to the small number of events (n=3).

Operative Characteristics. The procedural performance of IOC itself was safe, similar to data reported elsewhere[8]. Operative characteristics did not differ between the comparison groups, except for drains maintained postoperatively. The increased likelihood of Penrose drains left in the TCD catheter group is associated with the predicted risk of catheter dislocation. Conversely, the increased likelihood of Kehr drains left in the comparison group is explained by the greater proportion of CBD explorations in this group. Common bile duct exploration occurred proportionally more in the comparison group (20% vs. 3.6%, non-significant), with the only one that occurred in the TCD catheter group performed transcystically. Laparoscopic CBD exploration with choledochotomy is associated with higher successful duct clearance but also with higher complication rates when compared to a transcystically approach. [26] Open CBD exploration is associated with greater morbidity and has largely been replaced by laparoscopic and endoscopic procedures when available.[1, 3] These considerations led to the inclusion of CBD exploration in the final model to account as a potential confounder.

Postoperative Characteristics. Clearance was seen in 19% of asymptomatic choledocholithiasis patients in a recent report[27] assessed with MRCP. Collins et al. [18] reported a 26% spontaneous passage of stone assessed at 6 weeks through cholangiography using the TCD catheter. In light of important limitations discussed further, at least 3 patients out of 15 postoperative cholangiography through the TCD catheter (20%) in our cohort experienced asymptomatic passage of common bile ducts. It seems reasonable to pursue management decisions that postpone or avoid early CBD intervention. In the study by Hakuta et al.[27], endoscopic removal related complications occurred in 32% of patients (5.2% were severe pancreatitis). In our cohort, however, the TCD catheter maintenance did not seem to protect patients from complications despite having prevented ERCPs by confirming false-positive IOCs. Even in the setting of delayed ERCPs in cases of confirmed choledocholithiasis without the catheter, patients did not experience adverse events.

In our study, more MRCPs were conducted postoperatively in the comparative group (17 vs. 5,

p=0.203). However, there can potentially be patients that underwent MRCP before surgery (especially in the case of patients undergoing cholecystectomy in the setting of post biliary pancreatitis), which would further decrease this difference.

ERCPs and MRCPs did not find filling defects in 8/28 (28.57%) patients that remained with the TCD catheter. Three had no filling defects in repeated cholangiography through the catheter, resulting in an 11/28 (39.29%) false-positives or spontaneous clearance of CBD in our cohort. Determining the true nature of a positive IOC, such as whether it indicates a lack of flow of contrast into the duodenum or an actual filling defect remains discussable. Studies suggest that lack of flow of contrast into duodenum may be less specific for bile duct stones, since it may be due to a spasm of the sphincter of Oddi.[28] However, studies have found no difference in the positive predictive value of bile duct stones between the two types of IOC.[28, 29]

Lastly, a recent study[27] suggests there seems to be no difference in overall complications rates comparing expectant management (without TCD catheter) versus early endoscopic intervention. In fact, at least 5/83 (6%) of our cohort was followed with CBD stones asymptomatically.

Limitations. Our study has several limitations. In particular, the retrospective nature of the assessment that did not permit standardization in the management differences between the comparison groups. Additionally, intraoperative cholangiography descriptions were limited to reporting whether canulation had been successful and findings. Knowing whether there were difficulties in placing the catheter in the cystic duct could inform future decision-making, especially for patients where the catheter was displaced in the early postoperative period. The lack of standardization in the management of choledocholithiasis contemplating the maintenance of the TCD catheter postoperatively potentially reduced its benefit of repeating cholangiography and detecting false positive IOC findings. The wide confidence intervals for the estimated effects suggesting potentially small clinical effects are due to the relatively small number of complications and represent an important limitation. Finally, we acknowledge that the generalization of our findings is limited to settings with similar resources and characteristics where single-step approaches[1, 2, 5] that can dismiss the need for further CBD stone management are not feasible or are impractical.

CONCLUSION

Based on our findings we do not recommend the practice of maintaining the transcystic duct catheter in place postoperatively after positive intraoperative cholangiography due to its risks surpassing its benefits. That is particularly the case for post pancreatitis cholecystectomies, where a greater likelihood of false positives IOCs exists. Further studies could explore different measures to reduce unnecessary additional procedures in the context of filling defect findings during cholecystectomy with IOC. In the meantime, expectant follow-up seems a safer and more reasonable option, even in the context of limited availability of resources.

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DISCLOSURES

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REFERENCES

1. Manning A, Frazee R, Abernathy S, Isbell C, Isbell T, Regner J, et al. Protocol-Driven Management of Suspected Common Duct Stones. J Am Coll Surg. 2017;224(4):645-49.
2. Gurusamy KS, Giljaca V, Takwoingi Y, Higgie D, Poropat G, Stimac D, et al. Endoscopic retrograde cholangiopancreatography versus intraoperative cholangiography for diagnosis of common bile duct stones. The Cochrane database of systematic reviews. 2015(2):Cd010339.
3. Dasari BV, Tan CJ, Gurusamy KS, Martin DJ, Kirk G, McKie L, et al. Surgical versus endoscopic treatment of bile duct stones. The Cochrane database of systematic reviews. 2013(12):CD003327.
4. Kimura Y, Takada T, Kawarada Y, Nimura Y, Hirata K, Sekimoto M, et al. Definitions, pathophysiology, and epidemiology of acute cholangitis and cholecystitis: Tokyo Guidelines. Journal of hepato-biliary-pancreatic surgery. 2007;14(1):15-26.
5. Sun SX, Kulaylat AN, Hollenbeak CS, Soybel DI. Cost-effective Decisions in Detecting Silent Common Bile Duct Gallstones During Laparoscopic Cholecystectomy. Ann Surg. 2016;263(6):1164-72.
6. Ricci C, Pagano N, Taffurelli G, Pacilio CA, Migliori M, Bazzoli F, et al. Comparison of Efficacy and Safety of 4 Combinations of Laparoscopic and Intraoperative Techniques

for Management of Gallstone Disease With Biliary Duct Calculi: A Systematic Review and Network Meta-analysis. JAMA Surg. 2018;153(7):e181167.
7. Pesce A, Piccolo G, La Greca G, Puleo S. Utility of fluorescent cholangiography during laparoscopic cholecystectomy: A systematic review. World J Gastroenterol. 2015;21(25):7877-83.
8. Videhult P, Sandblom G, Rasmussen IC. How reliable is intraoperative cholangiography as a method for detecting common bile duct stones? : A prospective population-based study on 1171 patients. Surgical endoscopy. 2009;23(2):304-12.
9. Ford JA, Soop M, Du J, Loveday BP, Rodgers M. Systematic review of intraoperative cholangiography in cholecystectomy. Br J Surg. 2012;99(2):160-7.
10. Photi ES, El-Hadi A, Brown S, Swafe L, Ashford-Wilson S, Barwell J, et al. The Routine Use of Cholangiography for Laparoscopic Cholecystectomy in the Modern Era. JSLS. 2017;21(3).
11. O'Donovan AN, O'Sullivan G, Ireland A, FitzGerald E. Prospective trial of the role of fine bore intubation of the cystic duct at the time of operative cholangiography. J Am Coll Surg. 1997;184(3):262-4.
12. Cotton PB, Lehman G, Vennes J, Geenen JE, Russell RC, Meyers WC, et al. Endoscopic sphincterotomy complications and their management: an attempt at consensus. Gastrointestinal endoscopy. 1991;37(3):383-93.
13. Williams E, Beckingham I, El Sayed G, Gurusamy K, Sturgess R, Webster G, et al. Updated guideline on the management of common bile duct stones (CBDS). Gut. 2017;66(5):765-82.
14. Kaif M, Agrawal D, Sreenarasimhaiah J. Can clinical factors predict the need for intervention after a positive intraoperative cholangiogram? J Dig Dis. 2017;18(7):410-15.
15. Morris S, Gurusamy KS, Sheringham J, Davidson BR. Cost-effectiveness analysis of endoscopic ultrasound versus magnetic resonance cholangiopancreatography in patients with suspected common bile duct stones. PLoS One. 2015;10(3):e0121699.
16. Horwood J, Akbar F, Davis K, Morgan R. Prospective evaluation of a selective approach to cholangiography for suspected common bile duct stones. Annals of the Royal College of Surgeons of England. 2010;92(3):206-10.
17. Enochsson L, Swahn F, Arnelo U, Nilsson M, Lohr M, Persson G. Nationwide, population-based data from 11,074 ERCP procedures from the Swedish Registry for Gallstone Surgery and ERCP. Gastrointestinal endoscopy. 2010;72(6):1175-84, 84.e1-3.
18. Collins C, Maguire D, Ireland A, Fitzgerald E, O'Sullivan GC. A prospective study of common bile duct calculi in patients undergoing laparoscopic cholecystectomy: natural history of choledocholithiasis revisited. Ann Surg. 2004;239(1):28-33.
19. Lee TH, Hwang SO, Choi HJ, Jung Y, Cha SW, Chung IK, et al. Sequential algorithm analysis to facilitate selective biliary access for difficult biliary cannulation in ERCP: a prospective clinical study. BMC gastroenterology. 2014;14:30.
20. Maple JT, Ben-Menachem T, Anderson MA, Appalaneni V, Banerjee S, Cash BD, et al. The role of endoscopy in the evaluation of suspected choledocholithiasis. Gastrointestinal endoscopy. 2010;71(1):1-9.
21. DaVee T, Garcia J, TH. B. Precut sphincterotomy for selective biliary duct cannulation during endoscopic retrograde cholangiopancreatography. Annals of gastroenterology. 2012(25):291-302.
22. Davee T, Garcia JA, Baron TH. Precut sphincterotomy for selective biliary duct cannulation during endoscopic retrograde cholangiopancreatography. Annals of gastroenterology. 2012;25(4):291-302.

23. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240(2):205-13.
24. Chisholm PR, Patel AH, Law RJ, Schulman AR, Bedi AO, Kwon RS, et al. Preoperative predictors of choledocholithiasis in patients presenting with acute calculous cholecystitis. Gastrointestinal endoscopy. 2019;89(5):977-83.e2.
25. Krause TJ, Robertson FM, Liesch JB, Wasserman AJ, Greco RS. Differential Production of Interleukin 1 on the Surface of Biomaterials. Archives of Surgery. 1990;125(9):1158-60.
26. Bekheit M, Smith R, Ramsay G, Soggiu F, Ghazanfar M, Ahmed I. Meta-analysis of laparoscopic transcystic versus transcholedochal common bile duct exploration for choledocholithiasis. BJS Open. 2019;3(3):242-51.
27. Hakuta R, Hamada T, Nakai Y, Oyama H, Kanai S, Suzuki T, et al. Natural history of asymptomatic bile duct stones and association of endoscopic treatment with clinical outcomes. J Gastroenterol. 2020;55(1):78-85.
28. Singh G, Gupta PC, Sridar G, Katariya RN. Role of selective intra-operative cholangiography during cholecystectomy. The Australian and New Zealand journal of surgery. 2000;70(2):106-9.
29. Snow LL, Weinstein LS, Hannon JK, Lane DR. Evaluation of operative cholangiography in 2043 patients undergoing laparoscopic cholecystectomy: a case for the selective operative cholangiogram. Surgical endoscopy. 2001;15(1):14-20.

Table 1. Demographic and Preoperative Characteristics

		General	TCD Catheter Maintained	TCD catheter removed (Comparative Group)
n		**83 (100)**	**28 (33.73)**	**55 (66.27)**
Age (years)		48.47±19.03	49.08±17.36	48.37±19.41
Gender (female)		62 (74.7)	22 (78.6)	40 (72.7)
Comorbidities		58 (69.9)	23 (82.1)	35 (63.6)
	Hypertension	28 (33.7)	11 (39.3)	17 (30.9)
	Diabetes*	12 (14.5)	10 (35.7)	2 (3.6)
	Obesity	14 (16.9)	7 (25)	7 (12.5)
	Smoking	12 (14.5)	4 (14.3)	8 (14.5)
	Other	38 (45.8)	14 (50)	24 (43.6)
Pre-op signs/symptoms				
	Choluria	18 (25.7)	6 (24)	12 (26.7)
	Pale stools	12 (16.9)	6 (23.1)	6 (13.3)
	Jaundice	20 (28.2)	9 (34.6)	11 (24.4)
Pre-op laboratory findings				
	Amilase	80 [56, 190.5]	79.5 [65.75, 101.75]	95 [55, 210]
	Total Bilirrubin	0.6 [0.4, 1.7]	0.5 [0.4, 2.15]	0.75 [0.4, 1.7]
	Direct Bilirubin	0.4 [0.2, 1.25]	0.3 [0.2, 1.85]	0.4 [0.2, 1.2]
	Alkaline Phosphatase	126.5 [81.5, 195.75]	115.5 [74, 187.5]	131.5 [91.5, 200.75]
	GGT	232 [120, 446.5]	187 [85, 472]	232 [134, 384]
	Aspartate transaminase	57.5 [25.75, 158.75]	45 [19, 136]	78 [31, 160]
	Alanine transaminase	76.5 [43.25, 158.75]	58 [20, 159]	95 [51.5, 152]
	C-Reactive Protein	12.6 [5, 48.375]	21 [10.7, 52]	11.45 [3.575, 20.35]
Preoperative imaging with CBD diameter > 6mm		22 (26.5)	8 (28.6)	14 (25.5)

TCD = transcystic duct; GGT = Gamma Glutamyl transferase; CBD = Common Bile Duct;
Data displayed as n(%), mean ± std.dev., or median [25^{th} – 75^{th} percentile].
*Significant Fisher's exact test ($p<.05$).

Table 2. Operative Characteristics

		General	TCD Catheter Maintained	TCD catheter removed (Comparative Group)
n		**83 (100)**	**28 (33.735)**	**55 (66.265)**
Duration (minutes)		135 [105, 180]	137.5 [110, 175.25]	130 [105, 180]
Elective x Urgent				
	Elective	34 (41)	12 (42.9)	22 (40)
	Urgent	49 (59)	16 (57.1)	33 (60)
Preoperative Diagnosis				
	Symptomatic Gallstone	17 (20.5)	3 (10.7)	14 (25.5)
	Acute cholecistitis	18 (21.7)	9 (32.1)	9 (16.4)
	Post Billiary Pancreatitis	24 (28.9)	7 (25)	17 (30.9)
	CBD stones	24 (28.9)	9 (32.1)	15 (27.3)
IOC decision moment				
	Preoperative	69 (83.1)	24 (85.7)	45 (81.8)
	Intraoperative	14 (16.9)	4 (14.3)	10 (18.2)
IOC indication Reasoning				
	Clinical/Laboratory findings	15 (18)	8 (28.6)	7 (12.8)
	Pre-operative US, MRCP, or ERCP findings	28 (33.7)	8 (28.6)	20 (36.4)
	Transoperative anatomy	10 (12)	2 (7.1)	8 (14.5)
	Previous pancreatitis	20 (24.1)	7 (25)	13 (23.6)
	Not justified	10 (12)	3 (10.7)	7 (12.7)
Cystic Duct Manipulation		25 (30.1)	11 (39.3)	14 (25.5)
CBD Exploration		12 (14.5)	1 (3.6)	11 (20)
Drains left postoperatively*				
	None	43 (51.8)	6 (21.4)	37 (67.3)
	Penrose	32 (38.6)	21 (75)	11 (20)
	Kehr	8 (9.6)	1 (3.6)	7 (12.7)
Intraoperative Complication		3 (3.6)	0 (0.0)	3 (5.5)
Converted to Open Procedure		2 (2.4)	0 (0.0)	2 (3.6)

TCD = transcystic duct; CBD = Common Bile Duct; IOC = Intraoperative Cholangiography;
MRCP / ERCP = Magnetic Resonance / Endoscopic Retrograde Cholangiopancreatography;
Data displayed in n (%), median [25th, 75th percentile].
*Siginifcant Fisher's exact test ($p < 0.05$).

Table 3. Postoperative Charcateristics

		General	TCD Catheter Maintained	TCD catheter removed (Comparative Group)
n		**83 (100)**	**28 (33.735)**	**55 (66.265)**
Complications (Any)†*		20 (24.1)	11 (39.3)	9 (16.4)
Complications				
	None	63 (75.9)	17 (60.7)	46 (83.6)
	Minor	17 (20.5)	9 (32.1)	8 (14.5)
	Major	3 (3.6)	2 (7.1)	1 (1.8)
Post-op ERCP		48 (57.8)	18 (64.3)	30 (54.5)
Post-op MRCP		22 (26.5)	5 (17.9)	17 (30.9)
Hospital stay length (days)		10 [7, 16]	12 [7, 15.75]	10 [7, 16]
Number of post-op labs ordered		22 [12, 34]	20 [11.5, 27]	22 [12, 38.25]

TCD = transcystic duct; ERCP/MRCP = Endoscopic Retrograde/Magnetic Resonance Cholangiopancreatography;
Data displayed in n (%), mean ± std. dev. or median [IQR];
†Dichotomized; *Pearson Chi-square, $p<0.05$.

Table 4. Stratified Comparisons of Complications by TCD Catheter Maintenance

		Complications n=20		
		TCD Catheter Maintained n=28	TCD Catheter Removed (Comparative Group) n=55	RR (95%CI)
Complications (any)		11 (39.3)	9 (16.4)	2.4 (1.13, 5.1)ŧ
Age (years)				**2.29 (1.1, 4.78)**
	< 50 y.o.	5 (38.5)	1 (3.6)	10.77 (1.39, 83.14)
	≥ 50 y.o.	6 (40)	8 (29.6)	1.35 (0.58, 3.16)
Gender				**2.42 (1.1, 5.2)**
	Female	9 (40.9)	6 (15)	2.73 (1.12, 6.66)
	Male	2 (33.3)	3 (20)	1.67 (0.36, 7.61)
Comorbidities (any)*				**2.03 (0.98, 4.21)**
Yes		10 (43.5)	8 (22.9)	1.9 (0.88, 4.09)
No		1 (20)	1 (5)	4 (0.3, 53.47)
	Hypertension			**2.19 (1.07, 4.47)**
	Yes	5 (45.5)	6 (35.29)	1.29 (0.52, 3.21)
	No	6 (35.29)	3 (7.89)	4.47 (1.27, 15.8)
	Diabetes*			**1.71 (0.91, 3.23)**
	Yes	4 (40)	2 (100)	0.4 (0.19, 0.85)
	No	7 (38.89)	7 (13.21)	2.94 (1.2, 7.25)
	Obesity			**2.38 (1.15, 4.9)**
	Yes	1 (14.29)	2 (28.57)	0.5 (0.06, 4.33)
	No	10 (47.62)	7 (14.58)	3.26 (1.44, 7.40)
	Current Smoking			**2.41 (1.16, 4.99)**
	Yes	3 (75)	3 (37.5)	2 (0.69, 5.76)
	No	8 (33.3)	6 (12.77)	2.61 (1.02, 6.67)
	Other			**2.27 (1.09, 4.67)**
	Yes	8 (57.14)	6 (25)	2.29 (1, 5.23)
	No	3 (21.43)	3 (9.68)	2.21 (0.51, 9.64)
Preoperative imaging with CBD diameter > 6mm				**2.35 (1.12, 4.98)**
	Yes	3 (37.5)	4 (28.57)	1.32 (0.39, 4.44)
	No	8 (40)	5 (12.20)	3.28 (1.23, 8.75)
AST ≥ 3x reference value*				**1.88 (0.88, 4)**
	Yes	3 (42.86)	1 (6.25)	6.86 (0.85, 54.98)
	No	6 (40)	8 (29.63)	1.35 (0.58, 3.16)
Altered Alkhaline Phosphatase*				**1.57 (0.65, 3.8)**
	Yes	3 (30)	3 (15.79)	1.9 (0.47, 7.74)
	No	4 (36.36)	4 (26.67)	1.36 (0.43, 4.29)
Elective x Urgent				**2.44 (1.16, 5.11)**
	Elective	2 (16.67)	3 (13.64)	1.22 (0.24, 6.33)
	Urgent	9 (56.25)	6 (18.18)	3.09 (1.33, 7.19)
Preoperative Diagnosis				**2.74 (1.12, 6.71)**

	Symptomatic Gallstone	1 (33.3)	5 (35.71)	0.93 (0.16, 5.36)
	Acute cholecistitis	5 (55.56)	0 (0.0)	-
	Post Billiary Pancreatitis	1 (14.29)	0 (0.0)	-
	CBD stones	4 (44.4)	4 (26.67)	1.67 (0.55, 5.07)
IOC decision moment				**2.47 (1.87, 5.14)**
	Preoperative	7 (29.17)	7 (15.56)	1.88 (0.75, 4.72)
	Intraoperative	4 (100)	2 (20)	5 (1.45, 17.27)
IOC indication Reasoning				**2.88 (1.26, 6.55)**
	Clinical/Laboratory findings	4 (50)	0 (0.0)	-
	Pre-operative US, MRCP, or ERCP findings	3 (37.5)	5 (25)	1.5 (0.46, 4.85)
	Transoperative anatomy	2 (100)	2 (25)	4 (1.2, 13.29)
	Previous pancreatitis	1 (14.29)	0 (0.0)	-
	Not justified	1 (33.33)	2 (28.57)	1.67 (0.16, 8.48)
Cystic Duct Manipulation				**2.27 (1.1, 4.7)**
	Yes	3 (27.27)	4 (28.57)	0.96 (0.27, 3.4)
	No	8 (47.06)	5 (12.2)	3.86 (1.47, 10.12)
CBD Exploration				**3.05 (1.23, 7.6)**
	Yes	0 (0.0)	4 (36.36)	-
	No	11 (40.74)	55 (11.36)	3.58 (1.4, 9,2)
Drains*				**1.46 (0.68, 3.14)**
	None	2 (33.33)	4 (10.81)	3.08 (0.72, 13.3)
	Drains	9 (42.86)	4 (36.36)	1.18 (0.47, 2.97)
	Kher	0 (0.0)	1 (14.29)	-
Intraoperative Complication				**2.55 (1.16, 5.61)**
	Yes	0 (0.0)	1 (33.33)	-
	No	11 (39.29)	8 (15.38)	2.55 (1.16, 5.61)
Converted to Open Procedure				**2.6 (1.19, 5.72)**
	Yes	0 (0.0)	1 (50)	-
	No	11 (39.29)	8 (15.09)	2.6 (1.18, 5.72)
Post-op ERCP				**2.34 (1.08, 5.08)**
	Yes	3 (60)	4 (23.53)	2.55 (0.83, 7.78)
	No	2 (20)	4 (16)	1.25 (0.27, 5.78)
Post-op MRCP				**2.61 (1.22, 5.6)**
	Yes	3 (60)	4 (23.53)	2.55 (0.84, 7.79)
	No	8 (34.78)	5 (13.16)	2.64 (0.98, 7.11)

TCD = transcystic duct; GGT = Gamma Glutamyl transferase; ALT/AST = Alanine/Aspartate transaminase; CBD = Common Bile Duct; IOC = Intraoperative Cholangiography; US = Ultrasound; MRCP / ERCP = Magnetic Resonance / Endoscopic Retrograde Cholangiopancreatography;
Data displayed in n(%); ┼Crude estimate; Bold=Cochran-Mantel-Haenszel risk ratio (Adjusted RR).
*Non-Significant CMH test (p>0.05).

Table 5. Variables in the Exact Logistic Regression Model

Variable	B	Std. Error	OR (95% CI)	p-value
TCD Catheter Maintenance	1,675	0,690	5.34 (1.22, 29.83)	**0,022**
Age (years)	0,038	0,018	1.04 (1.01, 1.08)	**0,030**
Any Comorbidity	1,726	0,859	5.62 (1.31, 55.87)	**0,025**
Indication for Cholecistectomy				**0,035**
Symptomatic Gallstone*	-	-	-	
Acute cholecistitis	-0,904	0,842	0.41 (0.05, 2.67)	0,489
Post Billiary Pancreatitis	-2,951	1,226	0.05 (<0.01, 0.69)	**0,002**
CBD stones	-0,736	0,810	0.48 (0.07, 3.02)	0,597
Intraoperative Complications	0,985	1,606	2.68 (0.02, 159.42)	1,000
CBD Exploration	1,061	0,874	2.89 (0.38, 25.92)	0,411

TCD = transcystic duct; CBD = Common Bile Duct; ERCP = Endoscopic Retrograde Cholangiopancreatography
*Reference category

4 CONCLUSÃO

A manutenção do cateter colangiográfico na posição trancística após achado positivo de defeito de enchimento durante colangiografia intraoperatória foi associada a um aumento de mais de 5 vezes no risco de complicações comparado com a não-manutenção do mesmo, ajustado para potenciais fatores de confusão. O modelo construído levou em consideração o efeito de CPREs realizadas no pós-operatório, caso tenham sido evitadas ou não e as suas complicações associadas (especialmente pancreatite pós-CPRE).

Não houve diferença significativa no número de CPREs, de CRNMs e de exames laboratoriais realizados no período pós-operatório entre os grupos comparados. Da mesma forma, o tempo de internação hospitalar foi similar entre os grupos.

Baseado nos achados do estudo não se recomenda a prática de manutenção do cateter TC pós-operativamente após CIO positivas devido aos riscos superarem os potenciais benefícios. Essa conclusão é particularmente importante em casos de colecistectomias pós-pancreatite onde existe maior probabilidade de CIOs falso-positivas. Mais estudos podem explorar diferentes medidas para reduzir procedimentos adicionais desnecessários no contexto de defeitos de enchimento durante colecistectomias com CIO. Enquanto isso, manejo expectante parece ser seguro e a opção mais razoável em casos com limitada disponibilidade de recursos.

5 ANEXOS

5.1. Aprovação do Comitê de Ética

UFRGS - HOSPITAL DE CLÍNICAS DE PORTO ALEGRE DA UNIVERSIDADE FEDERAL

PARECER CONSUBSTANCIADO DO CEP

DADOS DA EMENDA

Título da Pesquisa: COLANGIOGRAFIAS INTRAOPERATÓRIAS COM DEFEITO DE ENCHIMENTO DO HOSPITAL DE CLÍNICAS DE PORTO ALEGRE

Pesquisador: GUILHERME GONCALVES PRETTO

Área Temática:

Versão: 2

CAAE: 98571118.5.0000.5327

Instituição Proponente: Hospital de Clínicas de Porto Alegre

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 3.376.263

Apresentação do Projeto:

Trata-se de emenda para solicitar prorrogação do estudo.

Objetivo da Pesquisa:

Trata-se de emenda para solicitar prorrogação do estudo.

Avaliação dos Riscos e Benefícios:

Não alterada.

Comentários e Considerações sobre a Pesquisa:

Foio enviada uma carta ao CEP, com a seguinte justificativa para a emenda:

"Não foi prevista uma redução do número de casos de colangiografias positivas com permanência do dreno transcístico nos anos de 2017 e 2016. Solicitamos prorrogação devido necessidade de revisar mais prontuários com objetivo de aumentar o número de casos afim de aumentar o poder estatístico das análises. Há intensão ainda de analisar padrões sazonais de alteração no número de colangiografias realizadas, positividade e condutas".

Considerações sobre os Termos de apresentação obrigatória:

Não se aplica.

Conclusões ou Pendências e Lista de Inadequações:

Os pesquisadores não informaram por quanto tempo será a prorrogação do estudo, ou seja, qual a nova data final.

Endereço: Rua Ramiro Barcelos 2.350 sala 2229
Bairro: Santa Cecília **CEP:** 90.035-903
UF: RS **Município:** PORTO ALEGRE
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De igual maneira, o processo de solicitação de prorrogação para os estudos foi simplificado recentemente, estando atualmente restrito à solicitação de um novo relatório no sistema AGHUse Pesquisa.

Para emitir o relatório siga os seguintes passos:

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b) No campo ‘relatório’ escolher a opção "Acompanhamento".

c) No campo ‘status’ escolher a opção "Prorrogação".

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e) O relatório será gerado em formato PDF e aparecerá registrado na aba Arquivos. Após aprovação do relatório pela Unidade de Assuntos Regulatórios de Pesquisa/CEP e Serviço de Gestão de Pesquisa, será emitida nova versão do relatório, pelo próprio sistema AGHUse Pesquisa, com as respectivas assinaturas eletrônicas das áreas que o avaliaram.

f) Uma vez aprovado o relatório, a nova data de término será atualizada no AGHUse Pesquisa e o projeto estará prorrogado.

Não se rá necessário submeter o relatório na Plataforma Brasil.

Considerações Finais a critério do CEP:
Ver conclusões deste parecer.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

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Continuação do Parecer: 3.376.263

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_1355966_E1.pdf	22/05/2019 17:31:04		Aceito
Outros	Carta_Justificativa.doc	22/05/2019 17:30:43	Thiago Bozzi de Araujo	Aceito
Outros	Carta_Adendo.doc	13/05/2019 20:58:28	Thiago Bozzi de Araujo	Aceito
Folha de Rosto	Folha_rosto.pdf	14/09/2018 17:47:10	Thiago Bozzi de Araujo	Aceito
Outros	delegacao_de_funcoes_para_a_equipe_de_pesquisa.pdf	14/09/2018 16:45:04	Thiago Bozzi de Araujo	Aceito
Outros	termo_dados.pdf	14/09/2018 16:44:44	Thiago Bozzi de Araujo	Aceito
Projeto Detalhado / Brochura Investigador	projeto.pdf	14/09/2018 16:42:30	Thiago Bozzi de Araujo	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

PORTO ALEGRE, 06 de Junho de 2019

Assinado por:
Marcia Mocellin Raymundo
(Coordenador(a))

Endereço: Rua Ramiro Barcelos 2.350 sala 2229
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Without DOI number:
Bates D (2002) The quality case for information technology in healthcare. Available at: http://www.biomedcentral.com/ 1472–6947/2/7. October 2002; Accessed 19 December 2002.

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Roy C (1988) Ultrasound of the abdomen (exercises in radiological diagnosis) Springer, Berlin

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White, ME, Choyke PL (1988) Duplex sonography of the abdomen. In: Grant EG, White EM (eds) Duplex sonography, Springer, New York,pp 129-190

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CONSENSUS STATEMENT ON SUBMISSION AND PUBLICATION OF MANUSCRIPTS

(Published in the June 2001 issue of *Surgical Endoscopy*, page 537)

Increasing problems of duplicate and fraudulent submissions and publications have prompted the editors of surgical journals, including Surgical Endoscopy, to support these overall principles of publication:

Duplicate Submission and Publication

In general, if a manuscript has been peer-reviewed and published, any subsequent publication is duplication. Exceptions to this general rule may be:

a) Prior publication in meeting program abstract booklets or expanded abstracts such as those published by the Surgical Forum of the American College of Surgeons or Transplantation Proceedings. However, these must be referenced in the final manuscript.
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The Internet raises special concerns. If data have previously appeared on the Internet, submission of those data for publication is considered duplication. If Internet publication follows journal publication, the journal publication should be clearly referenced. Some journals may provide early Internet publication of accepted peer reviewed papers which are subsequently published in that journal. This does not constitute duplication if both manuscripts are identical and covered by the same single copyright.

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The following activities are examples of fraudulent publication practices:

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While not intended as an all-inclusive document, these examples and guidelines should alert authors to potential problems that should be avoided when they are considering submission of a manuscript to a peer-reviewed journal.

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E. In Conclusion

This consensus statement is intended as a basic guide for authors. In the interest of promoting the highest ethics in surgical publishing and the surgical sciences, we ask that authors take these criteria into careful consideration when submitting a manuscript to a peer-reviewed surgical journal.