Aus der Klinik für Frauenheilkunde, Geburtshilfe und Reproduktionsmedizin

Universitätsklinikum des Saarlandes, Homburg / Saar

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Die laparoskopische Hysterektomie: Neue Erkenntnisse zu Operationstechniken, Einflussfaktoren und zum postoperativen Schmerzverlauf

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Inhaltsverzeichnis

1. Vorwort

Die folgenden wissenschaftlichen Abhandlungen zur laparoskopischen Hysterektomie entstanden im Rahmen meiner Tätigkeit als Doktorand der Klinik für Frauenheilkunde, Geburtshilfe und Reproduktionsmedizin in Homburg.

In Zusammenarbeit mit den Coautoren konnten im Wesentlichen folgende Fragestellungen bearbeitet werden:

a. Sollte bei der laparoskopischen Hysterektomie die Cervix in situ belassen oder entfernt werden? Welche der beiden Methoden birgt die geringste Gefahr von intra- und postoperativen Komplikationen?

b. Welchen Einfluss hat der Body Mass Index (BMI) auf intra- und postoperative Komplikationen bei der laparoskopischen Hysterektomie?

c. Wie wirken sich eine Nachbeatmung mit geöffnetem Nabeltrokar und eine zusätzliche Lidocaininfiltration an den Trokareinstichstellen auf den postoperativen Schmerzverlauf aus?

Die Ergebnisse der Datenanalysen konnten in internationalen Fachzeitschriften (peer-reviewed) publiziert und auf Kongressen vorgestellt werden.

Ein innerer Zusammenhang zwischen den Publikationen besteht insofern, dass sich alle Arbeiten mit dem intra- und postoperativen Verlauf der laparoskopischen Hysterektomie beschäftigen und sich die untersuchten Patientinnenkollektive teilweise überschneiden.

Im Folgenden werden die Arbeiten in einer erweiterten Zusammenfassung knapp auf Deutsch zusammengefasst. Hierbei werden nicht alle Details der erhobenen Daten vorgestellt. Weiterhin wird auch bei teilweise wörtlicher Übersetzung von Textpassagen nicht an allen Stellen auf die Originalpublikationen verwiesen, da diese in voller Länge in dieser Dissertation enthalten sind. Mein Eigenanteil an den Arbeiten wird ausführlich beschrieben. Auf eine erneute Zusammenfassung in englischer Sprache wird verzichtet. Die Rechte an den hier enthaltenen Publikationen liegen ausschließlich bei den jeweiligen Verlagen. Eine Vervielfältigung dieser Arbeit ist somit nicht zulässig, die Online-Version der Dissertation ist nicht durchsuchbar.

David Bardens im Dezember 2013

2. Erweiterte Zusammenfassung

2.1 Einleitung

Die Geschichte der Hysterektomie reicht zurück bis ins alte Griechenland, die erste Erwähnung findet die Operation in mehr als 2000 Jahre alten Manuskripten. (Baskett 2005) Bis heute ist die Hysterektomie eine der am häufigsten durchgeführten Operationen weltweit. (Baggish 2005) Seit den achtziger Jahren des letzten Jahrhunderts werden mehr und mehr Hysterektomien laparoskopisch durchgeführt, da sich gezeigt hat, dass diese im Vergleich zur abdominalen und zur vaginalen Hysterektomie einige Vorteile für die Patientinnen bietet. (Hwang et al. 2011; Nieboer et al. 2009; Sokol und Green 2009; Müller et al. 2010; Doğanay et al. 2011)

Es besteht bisher jedoch kein Konsens darüber, ob die Cervix bei einer laparoskopischen Hysterektomie in situ belassen werden sollte, sofern die letzten zytologischen Abstriche des Gebärmutterhalses vor der Operation unauffällig waren. Beim Belassen der Cervix mittels laparoskopischer supracervikaler Hysterektomie (LASH) bleibt die Integrität des Beckenbodens eher erhalten und der Vaginalpol muss nicht vernäht werden. Andererseits können persistierende Blutungsstörungen aus eventuell verbliebenem Restendometrium im Cervikalkanal eine Reoperation notwendig machen. Weiterhin verbleibt beim Belassen der Cervix ein minimales Risiko für die Entwicklung eines Cervixkarzinoms. (Sokol und Green 2009) Im Falle einer Entfernung der Cervix mittels totaler laparoskopischer Hysterektomie (TLH) können Dehiszenzen der Naht am Vaginalpol auftreten. In der ersten Studie, welche in dieser Dissertation vorgestellt wird, sollten beide Verfahren – LASH und TLH – bezüglich ihrer intra- und postoperativen Komplikationsraten verglichen werden. (Bardens et al. 2012)

Übergewicht und Adipositas sind laut Erhebungen der WHO ein weltweit zunehmendes Problem. (“Obesity: Preventing and Managing the Global Epidemic. Report of a WHO Consultation” 2000) In Deutschland sind nach Angaben des statistischen Landesamtes von Rheinland-Pfalz bereits über die Hälfte der Einwohner übergewichtig oder adipös. (“Daten Zur Gesundheit 2009 - Ergebnisse

Des Mikrozensus”) Deshalb ist es wichtig zu untersuchen, wie sich Übergewicht und Adipositas auf häufig durchgeführte Operationen auswirken. Es ist bekannt, dass Adipositas das Risiko für perioperative Thrombosen, Lungenembolien und Wundinfektionen erhöht. (DeMaria und Carmody 2005; Anaya und Dellinger 2006) Im Bezug auf laparoskopische gynäkologische Operationen wurde der Einfluss der Körperkonstitution bisher jedoch kontrovers diskutiert. Manche Autoren berichten von erhöhten Komplikations- und Laparokonversionsraten bei übergewichtigen Patienten (Heinberg et al. 2004; Bijen et al. 2011), während andere Autoren keine wesentlichen Unterschiede zwischen verschiedenen Gewichtsgruppen ausmachen können. (O’Hanlan et al. 2003; Mueller et al. 2010) In der zweiten Studie, welche an dieser Stelle vorgestellt wird, sollte der Einfluss des Body Mass Index (BMI) der Patientinnen auf die intra- und postoperativen Komplikationen der laparoskopischen Hysterektomie untersucht werden. (Bardens et al. 2013)

Nach laparoskopischen Operationen klagen viele Patienten über starke postoperative Schmerzen im Bereich des Abdomens und der Schultern. (McCloy et al. 2008; McGrath et al. 2004) Dies ist zum einen dem eigentlichen chirurgischen Trauma, andererseits aber auch der Irritation intraabdomieller Strukturen durch das bei der Laparoskopie insufflierte CO_2 geschuldet. (Jackson, Laurence, und Hill 1996; Korell et al. 1996; Alexander 1997; Wills und Hunt 2000) In der dritten Studie, die an dieser Stelle vorgestellt wird, sollte untersucht werden, ob eine Nachbeatmung (extended assisted ventilation, EAV) mit geöffnetem Nabeltrokar im Anschluss an die laparoskopische Hysterektomie einen Einfluss auf den postoperativen Schmerzverlauf und den postoperativen Schmerzmittelbedarf hat. Weiterhin wurde untersucht, ob eine zusätzliche Lidocaininfiltration an den Trokareinstichstellen den postoperativen Schmerzverlauf positiv beeinflussen kann. (Radosa et al. 2013)

2.2 Patientinnen und Methoden

Vor der Erhebung und Auswertung der Daten wurde ein Votum der Ethikkommission der Ärztekammer des Saarlandes eingeholt.

Alle laparoskopischen Hysterektomien wurden in Vollnarkose mit standardisierten Techniken durchgeführt, die bereits an anderer Stelle detailliert beschrieben wurden. (Radosa et al. 2013; Mueller et al. 2009)

Zu Bearbeitung der Fragestellungen ob die Cervix bei der laparoskopischen Hysterektomie in situ belassen werden sollte und wie sich der BMI auf den intra- und postoperativen Verlauf auswirkt, wurden die Daten aller Patientinnen ausgewertet, die zwischen September 2009 und April 2011 eine laparoskopische Hysterektomie aufgrund von benignen Erkrankungen am Universitätsklinikum des Saarlandes erhalten hatten. Patientinnen, bei denen der Verdacht auf eine maligne Erkrankung bestand wurden aus den Studien ausgeschlossen, während Präkanzerosen der Cervix nicht als Ausschlusskriterium gewertet wurden. Registriert wurden folgende Parameter: medizinische Vorgeschichte, Diagnosen, Größe, Gewicht, Geburtsdatum, Operationsdatum, Schnitt-Naht-Zeit, Blutverlust während der Operation (geschätzt durch den Operateur anhand der während der Operation abgesaugten Flussigkeitsmenge), perioperative Bluttransfusionen, gleichzeitig zur Hysterektomie durchgeführte Prozeduren (z.B. Adhäsiolyse, Cystoskopie), Gewicht des während der Operation entfernten Uterusgewebes, Hospitalisationsdauer, stationäre Wiederaufnahme und Reoperation sowie alle relevaten intra- und postoperativen Komplikationen und Auffälligkeiten, die bis zum Juli 2011 aufgetreten waren. Die Patientinnen wurden zur Auswertung des Einflusses der Körperkonstitution anhand der aktuellen BMI-Klassifikation der WHO in die Gruppen Untergewicht, Normalgewicht, Übergewicht und Adipositas eingeteilt. (“Obesity: Preventing and Managing the Global Epidemic. Report of a WHO Consultation” 2000)

Zur Untersuchung der Frage, ob eine Nachbeatmung mit geöffnetem Nabeltrokar sowie eine zusätzliche Lidocaininfiltraton an den Trokareinstichstellen einen Einfluss auf den postoperativen Schmerzverlauf und Schmerzmittelbedarf haben, wurde eine randomisierte prospektive Studie durchgeführt. Die Patientinnen, welche in die Studie eingeschlossen wurden, gaben nach vorheriger Aufklärung

ihr schriftliches Einverständnis zur Teilnahme. Einschlusskriterien waren: Alter 30-70 Jahre, ASA-Klassifikation I-II, laparoskopische Hysterektomie aufgrund von beningen Indikationen. Ausschlusskriterien waren: Ablehnung der Teilnahme an der Studie, ernsthafte intraoperative Komplikationen (wie Verletzung von Blase, Darm oder Ureter, Blutungskomplikationen mit Transfusionen, Hautemphysem), Laparokonversion, Unvollständigkeit der erhobenen Daten oder Unmöglichkeit der Datenerhebung bis 48 Stunden postoperativ. Eine Mindestanzahl von 86 Patienten pro Studiengruppe wurde errechnet, sodann wurde computergestützt eine Randomisationsliste erstellt, anhand derer die rekrutierten Patientinnen einer der Studiengruppen (Kontrolle, Nachbeatmung mit geöffnetem Nabeltrokar für 5 Minuten, Nachbeatmung mit geöffnetem Nabeltrokar für 5 Minuten und zusätzlich Infiltration der Trokareinstichstellen mit je 5ml Lidocain 0,4%) zugeordnet wurden. Alle Patientinnen erhielten nach der Operation eine standardisierte regelmäßige Schmerztherapie sowie eine standardisierte Bedarfsschmerzmedikation. Schmerzen in Abdomen und Schulter wurden 3, 24 und 48 Stunden nach der Operation mittels eines Fragebogens evaluiert. Der Schmerzmittelbedarf sowie Übelkeit und Erbrechen wurden 3 und 24 Stunden postoperativ registriert. Zusätzlich wurden die OP-Dauer, der intraoperative Gasverbrauch, die Hospitalisationszeit sowie postoperative Komplikationen registriert.

Die erhobenen Daten aller Studien wurden nach der Dokumentation in Tabellenkalkulationsprogrammen mit SPSS (SPSS Inc., IL, USA) bzw. GraphPad QuickCalcs Software (La Jolla, CA, USA) ausgewertet. Die Auswertung der BMI-Studie wurde in Zusammenarbeit mit dem Institut für medizinische Biometrie, Epidemiologie und medzinische Informatik der Universität des Saarlandes vorgenommen. P-Werte <0.05 wurden in den Studien zum Einfluss des BMI und zur Frage ob die Cervix in situ belassen werden sollte als statistisch signifikant angesehen. In der prospektiven Studie zur Nachbeatmung mit geöffnetem Nabeltrokar bzw. Lidocaininfiltration wurden p-Werte ≤ 0.01 als statistisch signifikant angesehen. Im Folgenden werden Daten in Form von Durchschnittswert ± Standardabweichung präsentiert.

2.3 Ergebnisse

Rahmendaten und Patientinnenkollektive

In der Zeit von September 2009 bis April 2011 wurden in der Universitätsfrauenklinik 200 laparoskopische Hysterektomien aufgrund von benignen Indikationen durchgeführt. Hiervon erhielten 108 Patientinnen eine totale laparoskopische Hysterektomie, in 92 Fällen wurde eine laparoskopische supracervikale Hysterektomie durchgeführt. Die häufigste Indikation für die Hysterektomie waren symptomatische benigne Tumoren des Uterus, wobei in 58,3% dieser Fälle gleichzeitig Blutungsanomalien aufgetreten waren. Zusätzlich zur Hysterektomie wurden in insgesamt 73% der Fälle weitere operative Interventionen wie Ovarialzystenentfernungen oder Adnexektomien durchgeführt. In 44,5% aller Fälle musste eine zusätzliche Adhäsiolyse, Neurolyse oder Ureterolyse erfolgen. Für 194 Patientinnen lagen genügend Daten vor um diese anhand der BMI-Klassifikation einzustufen. Der durchschnittliche BMI dieser Patientinnen betrug 26.8±6.2 kg/m^2. Lediglich 5 Patientinnen waren untergewichtig, diese wurden nach Rücksprache mit einem Statistiker von der weiteren Datenauswertung bzgl. des BMI ausgeschlossen um vergleichbare Gruppengrößen zu erreichen. Während des Beobachtungszeitraumes wurde eine Laparoskopie ungeplant aufgrund eines Uterusgewichtes von 2649g zur Laparotomie konvertiert. Dieser Fall wurde aus der weiteren statistischen Auswertung bezüglich Operationsdauer, Blutverlust, Uterusgewicht und Hospitalisationszeit ausgeschlossen. Es wurden keine weiteren intraoperativen Komplikationen registriert, insbesondere keine Verletzungen von Ureter, Blase oder Darm. In einem Fall wurde nach einer TLH ein Endometriumkarzinom als Zufallsbefund in der histologischen Untersuchung diagnostiziert. Diese Patientin erlitt postoperativ eine Venenthrombose und erhielt sekundär eine pelvine und paraaortale Lymphonodektomie sowie eine Radiatio. Der Fall wurde aus der weiteren Datenauswertung ausgeschlossen. Die Nachbeobachtungszeit dieses Patientinnenkollekivs betrug insgesamt 12.93±5.54 Monate. Das soeben beschriebene Patientinnenkollektiv wurde zur Auswertung der Fragestellungen bezüglich des Belassens der Cervix und des Einflusses des BMI auf die laparoskopische Hysterektomie herangezogen.

Bezüglich der prospektiven Schmerzstudie erfüllten im Rekrutierungszeitraum von Juli 2009 bis zum Dezember 2012 301 Patientinnen die Einschlusskriterien, wobei 295 Patientinnen ihr Einverständnis zur Teilnahme an der Studie erklärten. Zwei Patientinnen wurden aufgrund einer ungeplanten Laparokonversion aus der Studie ausgeschlossen, sodass insgesamt 293 Patientinnen in die Studiengruppen verteilt werden konnten. Weitere vier Patientinnen wurden wegen postoperativer Komplikationen oder oder nicht ausgefüllten Fragebögen ausgeschlossen, sodass letztendlich 95 Patientinnen aus der Kontrollgruppe, 96 Patientinnen aus der Nachbeatmungsgruppe und 94 Patientinnen aus der Gruppe Nachbeatmung + Trokareinstichstelleninfiltration ausgewertet werden konnten. Hiervon erhielten 184 Patientinnen eine TLH, bei 105 Patientinnen wurde eine LASH durchgeführt.

Laparoskopische supracervikale Hysterektomie (LASH) versus totale laparoskopische Hysterektomie (TLH)

Die Gruppe der Patientinnen, die eine supracervikale Hysterektomie erhielten, unterschied sich nicht signifikant von der TLH-Gruppe im Bezug auf Alter, Gewicht oder BMI. Die Follow-up-Zeiten sowie die Hospitalisationszeiten waren in beiden Kollektiven ebenfalls nicht signifikant unterschiedlich. Die Schnitt-Naht-Zeiten unterschieden sich signifikant voneinander ($p=0.004$), wobei für die TLH mehr Zeit benötigt wurde als für die LASH. Die geschätzten Blutverluste waren in beiden Gruppen mit maximal 300ml niedrig. Postoperativ zeigte sich, dass die Rate an Wundheilungsstörungen in der Gruppe der Patientinnen nach TLH signifikant höher war als in der Gruppe der Patientinnen nach LASH ($p=0.027$). Hierbei waren vor allem Wundheilungsstörungen des Vaginalstumpfes führend. Diese traten bei 12,2% aller Patientinnen nach TLH auf, wobei eine Patientin aufgrund einer Nahtdehiszenz reoperiert werden musste. Nach LASH erhielten zwei Patientinnen (2,2%) innerhalb der Nachbeobachtungszeit aufgrund persistierender Blutungsstörungen eine sekundäre Entfernung des Cervixstumpfes. Die beiden Gruppen unterschieden sich nicht im Bezug auf ernsthafte Komplikationen, die eine Wiederaufnahme und / oder Reoperation nötig machten.

Auswertung im Bezug auf verschiedene BMI-Gruppen

Patientinnen mit Normalgewicht, Übergewicht und Adipositas unterschieden sich nicht im Bezug auf die Indikationen, wegen derer eine Hysterektomie nötig

geworden war. Keine der Gruppen wurde bevorzugt für die supracervikale oder totale laparoskopische Hysterektomie ausgewählt. Die Gruppen unterschieden sich weiterhin nicht im Bezug auf gleichzeitig zur Hysterektomie durchgeführte Prozeduren (z.B. Ovarialcystenentfernungen), im Bezug auf das Alter, die Nachbeobachtungszeit, die Hospitalisationszeit oder das Gewicht des entfernten Uterusgewebes. Die Blutverluste unterschieden sich in den BMI-Gruppen signifikant voneinander ($p=0.017$), wobei bei übergewichtigen Patientinnen der größte Blutverlust zu verzeichnen war. Jedoch überstieg der Blutverlust bei keiner Patientin 300ml. Die Operationsdauer war in der Gruppe der normalgewichtigen Patientinnen am kürzesten (129.0±58.6 min), in der Gruppe der übergewichtigen Patientinnen etwas länger (135.4±46.9 min) und in der Gruppe der Patientinnen mit manifester Adipositas am längsten (154.6±64.2 min, $p=0.017$). Die Gesamtkomplikationsrate unterschied sich postoperativ signifikant zwischen den Gewichtsgruppen ($p=0.008$). In der Gruppe der übergewichtigen Patientinnen war die höchste Gesamtkomplikationsrate zu verzeichnen, in der Gruppe der Patientinnen mit manifester Adipositas war die Gesamtkomplikationsrate am niedrigsten. Im Bezug auf ernsthafte Komplikationen, die zu Wiederaufnahme oder Reoperation führten, unterschieden sich die Patientinnengruppen jedoch nicht signifikant.

Reduktion postoperativer Schmerzen durch eine Nachbeatmung mit geöffnetem Nabeltrokar und durch eine Nachbeatmung mit geöffnetem Nabeltrokar mit zusätzlicher Lidocaininfiltration an den Trokareinstichstellen

Die Operationszeit war bei Patientinnen, bei denen eine Nachbeatmung mit geöffnetem Nabeltrokar ± Lidocaininfiltration der Trokareinstichstellen durchgeführt worden war etwas länger im Vergleich zur Kontrollgruppe. Dieser Unterschied war jedoch nicht statistisch signifikant ($p=0.07$). Das Ausmaß der abdominellen Schmerzen war in beiden Interventionsgruppen nach 3 Stunden und nach 24 Stunden postoperativ signifikant niedriger als in der Kontrollgruppe ($p<0.01$ für die Gruppe mit Nachbeatmung und $p=0.01$ für die Gruppe mit Nachbeatmung und Lidocaininfiltration). Nach 48 Stunden war dieser Effekt nicht mehr feststellbar. Die zusätzliche Infiltration mit Lidocain an den Trokareinstichstellen zeigte jedoch im Bezug auf die abdominellen Schmerzen keinen Vorteil gegenüber der reinen Nachbeatmung mit geöffnetem Nabeltrokar. Im Bezug auf Schmerzen im Bereich der Schulter zeigte sich, dass die

Nachbeatmung mit geöffnetem Nabeltrokar das Schmerzniveau nach 24 und 48 Stunden signifikant gesenkt hatte ($p<0.01$). Auch hier konnte kein zusätzlicher Effekt durch eine Infiltration der Trokareinstichstellen mit Lidocain erzielt werden. Der Schmerzmittelverbrauch (Piritramid) war in beiden Interventionsgruppen nach drei Stunden postoperativ signifikant niedriger als in der Kontrollgruppe ($p<0.01$). 24 Stunden postoperativ blieb der Schmerzmittelverbrauch in beiden Interventionsgruppen weiterhin niedriger als in der Kontrollgruppe, dieser Unterschied war jedoch nicht mehr statistisch signifikant. Im Bezug auf postoperative Übelkeit und Erbrechen (PONV) konnten keine Unterschiede zwischen den Interventionsgruppen und der Kontrollgruppe festgemacht werden.

2.4 Diskussion

In der ersten hier vorgestellten Studie wurde die laparskopische supracervikale Hysterektomie (LASH) mit der totalen laparoskopischen Hysterektomie (TLH) verglichen. Hierbei war die Rate an intraoperativen Komplikationen bemerkenswert niedrig. In unserem Kollektiv von 200 Patientinnen musste nur eine Laparokonversion erfolgen, obwohl die Rate an zusätzlich zur Hysterektomie durchgeführten Adhäsiolysen – ein Hauptrisikofaktor für Konversionen (Park, Cho und Kim 2011) – mit 44,5% weitaus höher lag als die Adhäsiolyserate anderer Autoren. (Chopin et al. 2009) Wir schließen uns der Meinung anderer Autoren an, die niedrige Laparokonversionsraten auf standardisierte Prozeduren und die Durchführung der Operationen durch erfahrene Operateure mit hohen Fallzahlen zurückführen. (Mueller et al. 2009; Bojahr, Tchartchian und Ohlinger 2009) Es wurden keine Unterschiede zwischen LASH und TLH im Bezug auf schwerwiegende Komplikationen, die eine stationäre Wiederaufnahme und Reoperation bedingt hätten, festgestellt. Jedoch fanden sich in der Gruppe der Patientinnen nach TLH signifikant mehr Wundheilungsstörungen des Vaginalpols. Hierbei ist die von uns berichtete Rate an Wundheilungsstörungen vergleichbar mit der anderer Autoren. (Hwang et al. 2011) Das Problem von Nahtdehiszenzen des Scheidenstumpfes wurde in der Literatur bereits intensiv diskutiert und Geschlechtsverkehr vor dem vollständigen Verheilen des Vaginalpols scheint ein Haupttriggerfaktor zu sein. (Agdi et al. 2009; Iaco et al. 2006; Jeung et al. 2010) Eine sekundäre Entfernung des Cervixstumpfes nach LASH aufgrund persistierender Blutungsstörungen musste in 2,2% aller Fälle während des Nachbeobachtungszeitraumes erfolgen. Für die Durchführung der TLH wurde signifikant mehr Zeit benötigt als für die Durchführung der LASH. Es wurden keine weiteren nennenswerten Unterschiede zwischen beiden Verfahren festgestellt. Abschließend lässt sich feststellen, dass beiden Methoden sicher sind und mit einer minimalen Rate an intra- und postoperativen Komplikationen durchgeführt werden können. Die Patientinnen und Operateure sollten jedoch bei der Auswahl des Verfahrens berücksichtigen, dass das Belassen der Cervix in situ helfen kann Wundheilungsstörungen des Scheidenstumpfes zu vermeiden.

In der zweiten hier vorgestellten Studie wurden Daten zum Einfluss des Body Mass Index (BMI) auf die laparoskopische Hysterektomie präsentiert. Der durchschnittliche BMI des untersuchten Patientinnenkollektivs lag bei 26.8±6.2 kg/m^2, mehr als die Hälfte unserer Patientinnen waren übergewichtig oder adipös. Dies stützt die These dass Übergewicht und Adipositas ein zunehmendes Problem in Deutschland darstellen. Die Rolle des BMI im Bezug auf peri- und postoperative Komplikationen der laparoskopischen Hysterektomie wird jedoch kontrovers diskutiert. In der Literatur wird beschrieben, dass Übergewicht und Adipositas einen negativen Effekt auf den hormonellen Zyklus der Frau haben (Lash und Armstrong 2009) und dass Adipositas ein Risikofaktor für die Entwicklung von Uterusmyomen darstellt. (Terry et al. 2007) In unserem Patientinnenkollektiv konnten wir jedoch keine Unterschiede zwischen den BMI-Gruppen im Bezug auf die Indikationen für die Hysterektomie oder im Bezug auf die Notwendigkeit von simultan zur Hysterektomie durchgeführten Prozeduren feststellen. Die Gewichte des entfernten Uterusgewebes waren in der Gruppe der übergewichtigen und adipösen Patientinnen tendenziell höher als in der Gruppe der normalgewichtigen Patientinnen. Dieser Unterschied war jedoch statistisch nicht signifikant. Die Blutverluste waren zwischen den Gruppen signifikant unterschiedlich, wobei in der Gruppe der übergewichtigen Patientinnen der höchste Blutverlust zu verzeichnen war. Da der maximale Blutverlust jedoch nicht 300ml überstieg, ist die klinische Relevanz dieses Unterschiedes fraglich. Es scheint, dass Adipositas kein Risikofaktor für Blutungskomplikationen während laparoskopischer Hysterektomien ist. Manche Autoren berichten sogar von niedrigeren perioperativen Hb-Abfällen bei adipösen Patientinnen. (Mueller et al. 2010) Wir können die Ergebnisse anderer Studien bestätigen, wonach die Operationsdauer mit steigendem BMI zunimmt. (Heinberg et al. 2004; Chopin et al. 2009; Osler et al. 2011; Siedhoff et al. 2012) Dies scheint jedoch keinen wesentlichen Einfluss auf das Outcome der Patientinnen zu haben. Die postoperative Gesamtkomplikationsrate unterschied sich zwischen den BMI-Gruppen signifikant, wobei in der Gruppe der übergewichtigen Patientinnen die höchste Komplikationsrate und in der Gruppe der manifest adipösen Patientinnen die niedrigste Komplikationsrate zu beobachten war. Dies kann jedoch dadurch relativiert werden, dass sich die Gruppen nicht im Bezug auf ernsthafte Komplikationen unterschieden, die zu Wiederaufnahme und Reoperation geführt

hätten. Abschließend kann man feststellen, dass Übergewicht und Adipositas keinen wesentlichen negativen Effekt auf die laparoskopische Hysterektomie zu haben scheinen und dass die laparoskopische Hysterektomie eine auch bei übergewichtigen und manifest adipösen Patientinnen durchführbare und sichere Operationsmethode darstellt.

In der dritten, prospektiv randomisierten Studie wurde eine Reduktion der postoperativen Schmerzen nach laparoskopischer Hysterektomie durch eine verlängerte Nachbeatmung mit geöffnetem Nabeltrokar und durch eine zusätzliche Infiltration der Trokareinstichstellen mit Lidocain versucht. Es ist bekannt, dass die intraperitoneale Insufflation von CO_2 während Laparoskopien zur Entwicklung postoperativer Schmerzen – sowohl abdominell als auch im Bereich der Schulter – beiträgt, auch wenn der genaue pathophysiologische Mechanismus bisher unklar bleibt. (Coventry 1995; Yu et al. 2013; Aitola et al. 1998; Sammour et al. 2010; Dobbs et al. 1987; Jackson, Laurence und Hill 1996) Es wurden bereits verschiedene Versuche zur Beschleunigung der postoperativen CO_2-Elimination unternommen, hierunter eine Aspiration durch die Trokare mit simultaner Kompression der Bauchwand (Fredman et al. 1994) und die Anwendung von tiefen Beatmungen am Ende der Operation mit Beatmungsdrücken von bis zu 60mmHg. (Phelps et al. 2008; Sharami et al. 2010; Tsai et al. 2011) Diese Techniken haben sich zwar als effektiv erwiesen, die Anwendung hoher Beatmungsdrücke birgt jedoch das Risiko von Barotraumen und iatrogener Pneumothoraces. (Phelps et al. 2008; Tsai et al. 2011) Die von uns gezeigte Technik zur CO_2-Elimination erwies sich im Bezug auf die Reduktion postoperativer Schmerzen als vergleichbar effektiv wie die Beatmung mit hohen Beatmungsdrücken. Obwohl in den vorgestellten Daten keine signifikante Verlängerung der Operationszeit durch die zusätzliche Nachbeatmungszeit festgestellt wurde, könnte eine zusätzliche Nachbeatmungszeit in Zentren mit hohen Wechselzahlen im Bezug auf die Wirtschaftlichkeit relevant sein. Hier könnten weitere Studien mit verkürzter Nachbeatmungszeit bei geöffnetem Nabeltrokar zeigen, ob die von uns getestete Zeit von 5 Minuten bei ähnlicher Effektivität im Bezug auf die postoperativen Schmerzen weiter verkürzt werden könnte. Die Effektivität einer Applikation von Lokalanästhetika an Trokareinstichstellen nach Laparoskopien wird in der Literatur kontrovers diskutiert. (Benhamou et al. 1994; Helvacioglu und Weis 1992; Johnson et al.

1994; Ke et al. 1998) In unserer Studie konnte durch die lokale Infiltration der Trokareinstichstellen mit Lidocain im Bezug auf die postoperativen Schmerzen kein zusätzlicher Effekt zur CO_2-Elimination durch die Nachbeatmung mit geöffnetem Nabeltrokar gezeigt werden. Hier sind die Risiken und Nebenwirkungen einer Applikation von Lokalanästhetika sorgfältig gegen eine fragliche Schmerzreduktion abzuwägen.

3. Publikation 1: Comparison of Total and Supracervical Laparoscopic Hysterectomy for Benign Disease in a Collective of 200 Patients

Die Arbeit mit dem Titel „Comparison of Total and Supracervical Laparoscopic Hysterectomy for Benign Disease in a Collective of 200 Patients“ ist in Volume 28, Number 5 des Jahres 2012 im Journal of Gynecologic Surgery, herausgegeben von Mary Ann Liebert Inc., NY, USA, erschienen.

Auf den folgenden Seiten findet sich die Arbeit in der veröffentlichten Originalversion.

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Original Article

Comparison of Total and Supracervical Laparoscopic Hysterectomy for Benign Disease in a Collective of 200 Patients

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Abstract

Objective: The purpose of this study was to compare total laparoscopic hysterectomy (TLH) and laparoscopic supracervical hysterectomy (LASH) for benign disease, in terms of pre-, intra-, and postoperative findings and complications as well as necessary concomitant operative procedures. ***Design:*** This study was a retrospective review of 200 women who underwent LASH or TLH between September 2009 and April 2011. ***Materials and Methods:*** Statistical analysis and comparison of medical records were performed. Main outcome measures were patient characteristics, operating time, blood loss, uterine weight, concomitant procedures, length of stay, and intra- and postoperative complications. ***Results:*** TLH was performed in 108 cases, and 92 patients underwent LASH. The mean follow-up times were 12.5±5.4 months for TLH and 13.4±5.7 months for LASH. Suspected benign tumors of the uterus were the most frequent indication for both TLH and LASH (78% of all cases). The operating time for TLH was significantly longer than the time needed for LASH ($p=0.004$). The blood losses did not significantly differ. Concomitant operative procedures were necessary in 73% of all cases, mostly for the lysis of adhesions and the treatment of ovarian pathologies. Laparoconversion rate was 0.5%. The rate of wound healing problems was significantly higher in the group of patients who underwent TLH than in the group who underwent LASH ($p=0.027$). The groups did not differ in the rate of stationary readmission and repeat operation ($p=0.531$). ***Conclusions:*** Both procedures can be performed with a minimal rate of intra- and postoperative complications, even though removal of the cervix is associated with a higher rate of postoperative vaginal cuff wound healing problems. (J GYNECOL SURG 28:1)

Introduction

The ancient history of hysterectomy goes back to 2000-year-old Greek manuscripts, which describe the necessity of hysterectomy when a prolapsed uterus "has become black."[1] Since then, especially since the nineteenth century, new operating techniques for both total and subtotal removal of the uterus have continuously evolved and been improved. Today, hysterectomy is still one of the most frequently performed surgical procedures in the world.[2]

There are many different approaches to the removal of the uterus for benign disease, including abdominal (AH), vaginal (VH), laparoscopically assisted vaginal (LAVH), total (TLH), and subtotal (STLH/LASH) laparoscopic hysterectomy (LH).[3] It is widely accepted that of all these approaches, AH is associated with the longest hospital stay, the highest rate of infections, and the longest time to return to normal activities,[4] and that AH should be avoided whenever possible. Since the late 1980s and early 1990s, more and more hysterectomies are performed laparoscopically.[5] Laparoscopy enables the surgeon to inspect the peritoneal cavity and to perform concomitant procedures such as lysis of adhesions or treatment of endometriosis.[6] Mueller et al. showed in a recent retrospective study that TLH and LASH reduce the length of hospital stay and the amount of blood loss compared with LAVH and VH.[7] Moreover, LH seems to necessitate significantly fewer repeat operations than AH or VH.[8] However, a Cochrane review in 2009 found no evidence of benefits for LH versus VH, considering that the rate of substantial bleeding is lower and the operating time is shorter for VH.[4] In spite of this, there is still a lack of randomized controlled studies comparing the vaginal with the laparoscopic approach.

There has been a controversy over the removal of the cervix, given that the Papanicolaou smear test results are normal at the time of operation. For both TLH and LASH, there are method-specific problems that one should take into consideration. On the one hand, when leaving the cervix *in situ*, persistent bothersome menstrual bleeding may

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require secondary removal of the cervical stump. The risk of cervical carcinomas is low, with a rate of only 0.1% when leaving the cervix in place.[6] On the other hand, when removing the cervix and suturing the vaginal stump, vaginal cuff dehiscence may occur.

In this study, a closer look was taken at TLH and LASH. The characteristics and diagnoses of the patients selected for either TLH or LASH were compared, as were those approaches regarding necessary concomitant operative procedures, which had not yet been done in previous studies. In other studies, many of the concomitant procedures were excluded or not mentioned for the comparison of TLH to LASH for benign disease. Finally, an attempt was made to determine whether leaving the cervix *in situ* might promote or reduce any complications in the first months after surgery.

Materials and Methods

The study included all women who underwent TLH or LASH for benign disease at the Department for Obstetrics and Gynecology of the Saarland University Hospital between September 2009 and April 2011. Patients with suspected malignant diseases were excluded, whereas precancerosis of the cervix was not considered to be an exclusion criterion.

All of the operations were performed with the patient under general anesthesia, and patients stayed in the hospital for at least 3 days after the surgical intervention. The hysterectomies, TLH or LASH respectively, were performed using standardized surgical techniques that have already been described previously in detail elsewhere.[9] Vaginal cuff closure was performed by the laparoscopic route with figure-of-eight sutures.

The following data were collected pre-, intra-, and postoperatively: medical condition, diagnoses, weight, height, age, date of the procedure, blood loss during the operation (estimated by the surgeon from the amount of blood collected in the suction device), blood transfusions, operating time (time from the first incision or invasive procedure, respectively, to the last stitch), weight of the uterus tissue that was removed, concomitant procedures, length of hospital stay, readmission and repeat operation, as well as other relevant intra- and postoperative complications that occurred until July 2011. Wound healing problems of the vaginal cuff or cervical stump, respectively, were defined as infection and/or strong pain at the vaginal pole and/or bothersome polypous granulation tissue and/or bleeding of the operation site with an at least menstruation-like flow.

Statistical analysis

After obtaining an approval from the institutional review board, statistical analysis of the data was conducted by using SPSS 15.0 for Windows (SPSS Inc., Chicago, IL). Because none of the continuous variables approximated a normal distribution, the Mann–Whitney *U* test was used to evaluate significant differences. The categorical variables were evaluated with the χ^2 test with Yates correction. When >20% of the expected values in our contingency tables were <5, the *z*-test with Yates correction was used instead. A *p*-value <0.05 was considered to be statistically significant.

Results

During the study period, 108 women received TLH, whereas LASH was performed in 92 cases. The mean follow-up times were 12.5 months for TLH (SD 5.4) and 13.4 months for LASH (SD 5.7).

Only 1 procedure had to be converted from TLH to laparotomy because of the large uterus size (2649 g). That case was excluded for the evaluation of operating time, blood loss, uterine weight, and length of hospital stay.

Pre- and perioperative findings

An overview of the pre- and perioperative findings is shown in Table 1. The patients selected for TLH did not differ significantly from those selected for LASH in age, weight, or body mass index (BMI). The age range of the women selected for TLH (28.0–81.6 years) was higher than the age range of the women selected for LASH (31.2–68.4 years). The skin to skin operating time for TLH was significantly longer than the time needed to perform LASH ($p=0.004$). The estimated blood losses in the two groups were low, ranging to a maximum of only 300 mL. The mean hospitalization time turned out not to be significantly shorter for LASH, but it is noticeable that the range of the length of hospital stay was greater for patients undergoing TLH than the range evaluated for those who underwent LASH (3–10 days for LASH vs. 3–19 days for TLH). The weight of the uterine tissue that was removed was slightly lower in the TLH group, but there was no statistically relevant difference to the uterine weights excised by LASH.

Primary indications for surgery

Table 2 gives an overview of the findings and symptoms that physicians considered to be indications for surgery, after

Table 1. Pre- and Perioperative Findings

	LASH (n=*92*)	*TLH* (n=*108*)	p *value*
Age (years)	46.4±6.5 (range 31.2–68.4)	46.0±9.0 (range 28.0–81.6)	0.186
BMI (kg/m^2)	26.4±5.9 (range 16.8 – 42.6)	27.2±6.5 (range 17.1 – 48.4)	0.385
Operating time (min)[a]	126.4±53.9 (range 63–352)	145.7±58.9 (range 55–380)	0.004
Estimated blood loss (mL)[a]	71.6±64.3 (range 20–300)	81.9±75.9 (range 20–300)	0.618
Length of hospital stay (days)[a]	5.7±1.6 (range 3–10)	6.3±2.3 (range 3–19)	0.131
Uterine weight (g)[a]	216.0±231.8 (range 36–1111)	202.8±193.6 (range 38.5–1365)	0.439

Data presented as Mean±standard deviation.
[a]One case excluded because of conversion to laparotomy.
LASH, laparoscopic supracervical hysterectomy; TLH, total laparoscopic hysterectomy; BMI, body mass index.

Table 2. Primary Indications for Surgery

	LASH (n=*92*)	*TLH* (n=*108*)	p *value*
Suspicion of uterine leiomyomas and/or adenomyosis uteri	85.9% (79)	71.3% (77)	0.021
Menstrual bleeding disorders[a]	67.4% (62)	54.6% (59)	0.090
Abnormal Papanicolaou	-	18.5% (20)	-
Postmenopausal uterine bleeding	2.2% (2)	2.8% (3)	0.855
Other[b]	33.7% (31)	34.3% (37)	0.947

Total numbers of patients in parentheses. Summations >100% because of comorbidity.
[a]Hypermenorrhea, dysmenorrhea, polymenorrhea, menorrhagia, metrorrhagia, menometrorrhagia.
[b]Other indications: cancerophobia, benign ovarian cysts, endometriosis, pelvic organ prolapse.
LASH, laparoscopic supracervical hysterectomy; TLH, total laparoscopic hysterectomy.

taking the medical histories and examining the patients in the clinic.

Suspected benign tumors of the uterus were by far the most frequent indication for both TLH and LASH, although those patients were significantly more often planned for LASH ($p=0.021$). In women with suspected adenomyosis uteri and/or uterine leiomyoma, menstrual bleeding anomalies were comorbid in 58.3% of the cases. In total, bleeding anomalies were present in 67% (53) of the cases designated for supracervical hysterectomy and in 50.6% (79) of the cases planned for total hysterectomy ($p=0.090$). Patients with cervical precancerosis were planned for TLH.

Concomitant operations and procedures

A detailed overview of concomitant operations and procedures can be found in Table 3. In addition to the hysterectomy, other surgical interventions were necessary in 73% of all cases. Adhesiolysis, neurolysis, and ureterolysis were the most frequent concomitant procedures (necessary in as often as 44.5% of all cases), followed by the removal of ovarian cysts, and colposuspension. Although not statistically different, it is noticeable that adnexectomy was performed more often with TLH than with supracervical hysterectomy ($p=0.070$).

Intra- and postoperative complications

During the study period, none of the patients died as a result of intra- or postoperative complications. No iatrogenic injuries to the intestine, urinary tract, or vessels occurred. Only one operation (0.5%) had to be converted from laparoscopy to laparotomy, because of the large uterus size (2649 g). That patient lost ~1500 mL of blood during the hysterectomy (hemoglobin [Hb] 6.7 g/dL) and received two blood transfusions after the operation. That case was excluded for the statistical evaluation of postoperative complications. No other remarkable intraoperative complications occurred in this series of 200 laparoscopies.

Table 4 gives an overview of the postoperative complications. The rate of wound healing problems was significantly higher in the group of patients who underwent TLH than in the group who underwent LASH ($p=0.027$). However, the groups did not differ in the rate of serious complications that required stationary readmission and repeat operation ($p=0.531$). Secondary removal of the cervical stump because of troublesome, persistent menstrual bleeding, had to be performed after 2.2% of all supracervical hysterectomies during the follow-up period, something that was method specific for LASH.

As a secondary finding, endometrial cancer was detected by the pathologist after the operation in 1 case in the TLH group (finally pT1a pN0 V1 G2). The patient was 59.5 years old and postoperative muscle vein thrombosis was diagnosed 1 day after surgery. The diagnosis necessitated secondary pelvic and para-aortal lymphonodectomy as well as local radiation therapy. That case was not excluded for the evaluation of postoperative complications because that diagnosis had not been expected when planning the hysterectomy, as the case history and ultrasound findings were unremarkable.

Discussion

In this study, TLH was compared with LASH for benign disease.

Table 3. Concomitant Operations and Procedures

	LASH (n=*92*)	*TLH* (n=*108*)	p *value*
Total of concomitant procedures	70.7% (65)	75% (81)	0.265
Adhesiolysis, ureterolysis, neurolysis	46.7% (43)	42.6% (46)	0.656
Excision of ovarian cysts or hydatids	17.3% (16)	18.5% (20)	0.982
Colposuspension	18.5% (17)	12% (13)	0.283
Adnexectomy	6.5% (6)	15.7% (17)	0.070
Excision of endometriosis	12% (11)	7.4% (8)	0.394
Salpingectomy	5.4% (5)	8.3% (9)	0.601
Other[a]	16.3% (15)	20.4% (22)	0.579

Total numbers of patients in parentheses.
[a]Other: hysteroscopy, cystoscopy, scar revision, dilatation and curettage (D&C), laser ablation of genital warts.
LASH, laparoscopic supracervical hysterectomy; TLH, total laparoscopic hysterectomy.

Table 4. Postoperative Complications

	LASH (n=*92*)	*TLH* (n=*107*)[a]	p *value*
Total of postoperative complications requiring stationary readmission and repeat operation	4.4% (4)	7.5% (8)	0.531
Total of wound healing problems	3.3% (3)	13.1% (14)	0.027
• Wound healing problems of the cervical stump or vaginal cuff respectively[b]	Ambulatory manageable: 1.1% (1)	Ambulatory manageable: 10.3% (11) Requiring repeat operation: 1.9% (2)	
• Wound dehiscences and hematomata at trocar sites	2.2% (2)	0.9% (1)	
Postoperative functional abdominal pain and dyspareunia[c]	2.2% (2)	5.6% (6)	0.393
Peritoneal adhesions and pseudocysts requiring operative revision	2.2% (2)	3.7% (4)	0.840
Secondary removal of the cervix because of persistent vaginal bleeding	2.2% (2)	-	-
Postoperative detection of endometrial cancer as a secondary finding, requiring repeat operation and radiation therapy[d]	0	0.9% (1)	0.911
Postoperative abdominal bleeding requiring revision and blood transfusion	0	0.9% (1)	0.911

Total numbers of patients in parentheses.
[a]One case excluded because of conversion to laparotomy.
[b]Defined as infection and/or strong pain at the vaginal pole and/or bothersome polypous granulation tissue and/or bleeding of the operation site with an at least menstruation-like flow.
[c]Peritoneal adhesions requiring operative revision or pathologies of the vaginal cuff or cervix excluded.
[d]See "Results" section for a detailed description of the case.
LASH, laparoscopic supracervical hysterectomy; TLH, total laparoscopic hysterectomy.

The patient collectives selected for TLH or LASH did not differ significantly in age, weight, or BMI. Those patient characteristics were very similar to other collectives recently reported for the assessment of the same subject.[9–11]

This study confirms the experience of Mueller et al. and Boosz et al., who described that weights of uteri excised using the LASH technique tend to be a little bit higher, despite the uterine weights in the current study being lower than theirs. We also think that this might be a result of the nonrandomized, retrospective design of the current studies.[9,10]

The skin to skin operating time in this study was a little higher than that reported by some other authors,[5,9,12] which may be caused by the fact that this study did not exclude concomitant procedures. This study appears to be the first published detailed comparison of the concomitant procedures that are necessary during TLH and LASH for benign uterine disease. In other studies, many of the concomitant procedures were excluded or not mentioned for the comparison of TLH with LASH. That is why the operating time reported in this study may be closer to reality. The rate of other procedures performed during laparoscopic hysterectomy was very high. This may have three main causes. First, the surgeon can select patients with comorbid pathologies (e.g., cysts of the ovaries) for the laparoscopic approach. When laparoscopy is performed, access to the peritoneal cavity can be used to treat such a comorbid pathology. Second, during laparoscopy, unexpected pathologies can be visualized and treated. Third, adhesiolysis may be necessary to visualize and access the operation site. Adhesiolysis, ureterolysis and/or neurolysis were by far the most common concomitant procedures in this collective and needed to be performed in 44.5% of all cases. This is almost double the adhesiolysis rate that Chopin et al. reported for a collective of 1460 patients who underwent TLH.[13] The difference may be partially explained by this study's inclusion of ureterolysis and neurolysis. The second reason for concomitant procedures was the existence of ovarian pathologies, whereas adnexectomy was performed more often with TLH than with LASH (not statistically significant, $p=0.070$). This might be one reason for the operating time observed here being significantly longer for TLH than for LASH ($p=0.004$); in addition the total rate of concomitant procedures was slightly higher in the TLH group (75% vs. 70.7% in the LASH group).

A total laparoconversion rate of only 0.5% was observed in this series of 200 laparoscopic hysterectomies (0.93% in the TLH group, no cases in the LASH group). That rate is very low when compared with the conversion rates observed by Harmanli et al. in a collective of >1000 patients (4.1% for LASH and 5.8% for TLH).[11] The reason for their conversion rates being so high might be that a total of 48 gynecologists contributed to their study sample and that the number of cases per surgeon varied exorbitantly. In our study, the operations were performed by only a few well-experienced laparoscopists. Park et al. recently reported a conversion rate of 8% in a collective of 288 patients who underwent TLH.[14] They identified pelvic adhesions as a main risk factor for laparoconversion in their clinic. Considering that this study's rate of adhesiolysis was extremely high and the conversion rate was 16-fold lower, it is questionable how their conversion rates can be explained. This study bears out the experience of other authors that conversion rates can be low when using standardized procdures and well-trained surgeons.[9,15] No other intraoperative complications occurred, especially no iatrogenic injuries to the bowel or urinary tract.

No differences were observed between TLH and LASH in terms of stationary readmission and reoperation ($p=0.531$).

However, there was a high rate of wound healing disorders of the vaginal cuff in the TLH group that occurred in as many as 12.2% of all women, whereas 1.9% of all TLH patients needed resuturing of the vaginal pole. The vaginal cuff complication rate in this study was comparable to the rate recently reported by Hwang et al. for a collective of 471 patients.[5] In contrast, the total number of wound healing problems in the LASH group was significantly lower ($p=0.027$). Vaginal cuff dehiscence has been extensively discussed in the literature, and sexual intercourse before complete healing seems to be the main trigger event in young patients.[16, 17] It remains unclear why the risk of cuff dehiscence after LH is higher than with AH, and there is no consensus about the best stump-suturing technique.[18] Method-specific for LASH, secondary removal of the cervical stump was necessary in 2.2% of all cases during this study's follow-up time. No other statistically relevant differences between TLH and LASH were found.

Conclusions

Both total and subtotal LH can be performed safely, with a minimal rate of intra- and postoperative complications, as long as the patients are selected carefully and the surgeons are experienced and welltrained.

However, when deciding between LASH and TLH, the patient and the surgeon should consider that leaving the cervix *in situ* might reduce postoperative wound healing problems of the vaginal cuff.

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Disclosure Statement

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3.1 Beschreibung des Eigenanteils an Publikation 1

Die Grundidee zum Vergleich der laparoskopischen supracervikalen Hysterektomie mit der totalen laparoskopischen Hysterektomie am Universitätsklininikum des Saarlandes stammt von Herrn Priv.-Doz. Dr. med. Ingolf Juhasz-Böss und Prof. Dr. med. Erich-Franz Solomayer. Ich selbst habe die Datenerhebung zur Studie in Absprache mit Herrn Priv.-Doz. Dr. med. Ingolf Juhasz-Böss vorgenommen. Die Operationen der Patientinnen wurden zum Großteil von Herrn Professor Dr. med. Erich-Franz Solomayer, Herrn Professor Dr. med. Achim Rody, Herrn Priv.-Doz. Dr. med. Ingolf Juhasz-Böss und Herrn Dr. med. Sascha Baum durchgeführt. Die Auswertung der Daten, die Manuskripterstellung sowie die Einreichung des Manuskriptes beim Journal of Gynecologic Surgery erfolgten durch mich selbst in enger Abstimmung mit Herrn Priv.-Doz. Dr. med. Ingolf Juhasz-Böss. Alle Autoren hatten vor der Einreichung des Manuskriptes die Gelegenheit, den Entwurf zu lesen und Änderungs- sowie Ergänzungsvorschläge zu äußern und machten davon auch Gebrauch.

3.2 Aus Publikation 1 hervorgegangene Kongresspräsentationen

Vorträge

16th World Congress on Obstetrics, Gynecology and Infertility, Singapore, July 2012: „Laparoscopic hysterectomy: should the cervix be left in situ? A comparison of total laparoscopic hysterectomy and laparoscopic supracervical hysterectomy in a collective of 200 patients.“ (Referent: David Bardens)

Poster

22nd Annual Congress of the European Society of Gynecological Endoscopy (ESGE), Berlin, October 2013: „Laparoscopic hysterectomy for benign disease: should the cervix be left in situ?” (Autoren: Bardens D., Solomayer E., Radosa J., Rody A., Baum S., Juhasz-Böss I.)

59. Kongress der Deutschen Gesellschaft für Gynäkologie und Geburtshilfe, München, Oktober 2012: „Sicherheit der laparoskopischen Hysterektomie: LASH versus TLH in einem Kollektiv von 200 Patientinnen.“ (Autoren: Bardens D., Solomayer E., Rody A., Baum S., Juhasz-Böss I.)

4. Publikation 2: The impact of the body mass index (BMI) on laparoscopic hysterectomy for benign disease

Die Arbeit mit dem Titel „The impact of the body mass index (BMI) on laparoscopic hysterectomy for benign disease“ ist am 11.Oktober 2013 online in Archives of Gynecology and Obstetrics, herausgegeben vom Springer Verlag, Berlin, Deutschland, erschienen. Die Printausgabe lag zum Zeitpunkt der Abfassung dieser Dissertation noch nicht vor.

Auf den folgenden Seiten findet sich die Arbeit in der veröffentlichten Originalversion.

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GENERAL GYNECOLOGY

The impact of the body mass index (BMI) on laparoscopic hysterectomy for benign disease

David Bardens · Erich Solomayer · Sascha Baum · Julia Radosa · Stefan Gräber · Achim Rody · Ingolf Juhasz-Böss

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Abstract
Purpose To investigate the influence of the body mass index (BMI) on laparoscopic hysterectomy, including all intra- and postoperative findings and complications.
Methods We reviewed and analyzed the medical records of 200 patients who underwent laparoscopic hysterectomy for benign disease at the Saarland University Hospital. The patient collective was subdivided into four weight groups on the basis of the current WHO BMI classification. Data analysis was carried out by a professional statistician.
Results Over half of the women screened were overweight or obese. The operating times increased together with the BMI ($p = 0.017$). Blood losses differed significantly between the weight groups ($p = 0.027$), but ranged to a maximum of only 300 ml. One laparoconversion had to be performed. No other intraoperative complications occurred. During our follow-up time of 13.2 ± 5.4 months, the overall rate of postoperative complications differed significantly between the weight groups ($p = 0.008$). The group of overweight women had the highest rate of complications and the group of obese women had the lowest. However, the rate of women who required readmission and reoperation was not elevated in the overweight group.
Conclusion Laparoscopic hysterectomy is a safe and feasible method even in obese and morbidly obese patients. Overweight and obesity increase the time needed to perform laparoscopic hysterectomy but do not seem to relevantly influence the rate of major intra- or postoperative complications.

Keywords Body mass index (BMI) · Laparoscopy · Hysterectomy · Obesity · Overweight

Introduction

Excess of body weight has become a global epidemic. According to the WHO, the prevalence of overweight and obesity is increasing worldwide at an alarming rate [1]. In the US, approximately two-thirds of all adults are overweight or obese [2]. Obesity is associated with several comorbidities such as coronary heart disease and diabetes mellitus [3].

Considering those facts, it is crucial to investigate the influence of obesity on common surgical procedures. It is known that obese patients have a higher incidence for perioperative deep venous thrombosis and pulmonary embolism [3]. Furthermore, obesity has been identified as a risk factor for surgical site infection [4]. But studies investigating the role of overweight and obesity in laparoscopic gynecological surgery have provided inconsistent results. Some authors found elevated rates of complications and laparoconversions in the obese [5, 6], while others suggest that there are no relevant differences between the weight groups [7, 8].

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The aim of this study was to examine the impact of the body mass index (BMI) on intra- and postoperative complications for patients undergoing laparoscopic hysterectomy for benign disease.

Materials and methods

The study included all women who underwent laparoscopic hysterectomy for benign disease at the Saarland University Hospital between September 2009 and April 2011. Patients with suspected malignancies were excluded. All operations were carried out under general anesthesia in an inpatient setting, using standardized surgical techniques for total laparoscopic hysterectomy (TLH) and laparoscopic supracervical hysterectomy (LASH) [9]. Vaginal cuff closure was carried out laparoscopically with figure-of-eight sutures. We already published a comparison of total and supracervical laparoscopic hysterectomy based on data of the same patient collective [10].

The following observations were registered pre-, intra-, and postoperatively: medical history, age, body mass index (calculated as the weight in kilograms divided by the square of the height in meters), indications for hysterectomy, date of the operation, skin-to-skin operating time, blood loss, weight of the uterus tissue that was removed, concomitant procedures, intraoperative complications, other relevant findings that were noted in the surgical report, histological findings, length of hospitalization, readmission and reoperation, as well as all follow-up visits and postoperative complications that occured up to July 2011. All of the patients had follow-up visits either at our hospital or at their gynecologist's office. The patients were instructed to return to our hospital in case of any complications. The gynecologists were instructed to report all women with irregularities and complications during follow-up visits and to send those patients back to our hospital for a repeat examination.

After obtaining approval of the institutional review board, the collective was subdivided into four weight groups on the basis of the current WHO BMI classification [1]. Patients with a BMI lower than 18.50 kg/m^2 were classified as underweight. Patients with a BMI ranging from 25 to 29.99 kg/m^2 were classified as overweight. Patients with a BMI of 30 kg/m^2 or higher were classified as obese. All other patients were considered to be at normal weight.

Subsequently, the data analysis was carried out by a professional statistician using SPSS 19.0 for Windows (SPSS Inc., Chicago, IL). Differences between categorical variables were evaluated using the Chi-square test and the Fisher's exact test. Continuous variables were evaluated by using the Kruskal–Wallis analysis of variance on ranks. A p value <0.05 was considered to be statistically significant.

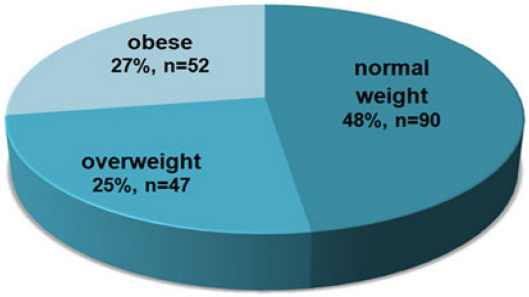

Fig. 1 BMI distribution in the patient collective. *BMI* body mass index

Results

BMI distribution

During the study period, 200 women underwent laparoscopic hysterectomy for benign disease during the study period. The hysterectomy was carried out supracervically in 92 cases; total laparoscopic hysterectomy was performed in 108 cases. Sufficient data about the BMI was available for 194 patients. The mean BMI was 26.8 ± 6.2 kg/m^2. Of the 194 patients, only five women were underweight. After consulting a statistician we excluded those five women from our data analysis to ensure comparable group sizes for the provision of reliable findings. Figure 1 shows the weight distribution in the patient collective that was finally included in the data analysis. None of the weight groups was preferably selected for either total or supracervical hysterectomy ($p = 0.323$).

Indications for hysterectomy and concomitant procedures

In our analysis, we did not find any statistically significant differences between the BMI subgroups in terms of the primary indications for laparoscopic hysterectomy. Particularly none of the subgroups presented with increased rates of bleeding anomalies ($p = 0.548$), uterine fibroids ($p = 0.960$), premalignant conditions of the cervix ($p = 0.120$) or postmenopausal bleedings ($p = 0.101$). Moreover, we observed no differences between the groups in matters of the rates or the kinds of operations and procedures that were performed in addition to the hysterectomy.

Findings in relation to BMI subgroups

Table 1 shows part of our findings in relation to the BMI. The groups did not differ significantly from each other with regard to follow-up times, age, length of stay, and the weight of the resected uterus tissue. The blood losses were

Table 1 Findings in relation to BMI subgroups

	Normal weight ($n = 90$)	Overweight ($n = 47$)	Obese ($n = 52$)	p value
BMI (kg/m^2)	22.3 ± 1.6	27.2 ± 1.6	35.2 ± 4.8	–
Follow-up time (months)	13.2 ± 5.9	12.5 ± 5.4	13.9 ± 4.9	0.455
Age (years)	45.4 ± 5.7	47.8 ± 9.4	45.9 ± 9.1	0.299
Length of stay (days)	5.8 ± 2.2	6.2 ± 2.1	5.8 ± 1.6	0.536
Weight of the resected uterus tissue (g)	194.4 ± 191.6	237.0 ± 246.3	224.6 ± 227.4	0.692
Blood loss (ml)	61.3 ± 56.0	108.8 ± 84.3	91.0 ± 80.9	0.027
Operating time (min)	129.0 ± 58.6	135.4 ± 46.9	154.6 ± 64.2	0.017

Data presented as mean ± standard deviation. Statistical test used: ANOVA

BMI body mass index

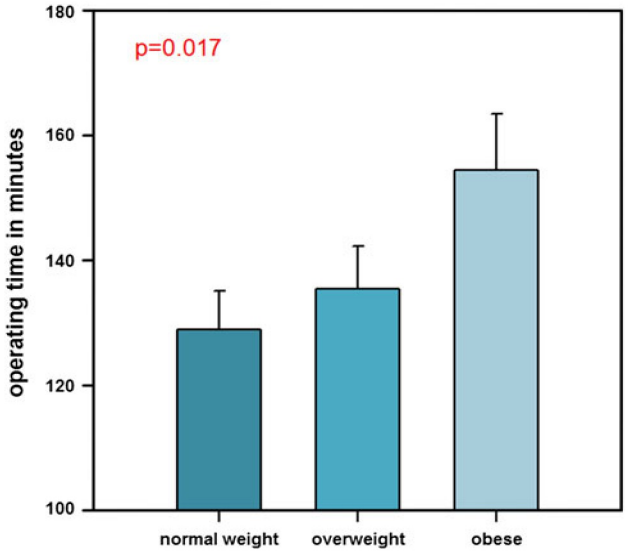

Fig. 2 Operating time in relation to BMI subgroups. Plot showing the operating times in relation to the BMI subgroups. The underlying data can be found in Table 1. *Error bars* represent the standard error of the means. *BMI* body mass index

low (range 20–300 ml) but differed significantly between the groups ($p = 0.027$). Overweight patients had the highest amount of blood loss. The operating times increased together with the BMI and the differences between the groups were statistically significant ($p = 0.017$). A graphical presentation of the operating times can be found in Fig. 2.

Intra- and postoperative complications in relation to BMI subgroups

During the study period, one of the operations had to be converted from laparoscopy to laparotomy. The patient's uterus weighed over 2.6 kg and the conversion seems not to be correlated with the woman's body type. No other intraoperative complications occurred.

Table 2 Intra- and postoperative complications in relation to BMI subgroups

	Normal weight ($n = 90$) (%)	Overweight ($n = 47$) (%)	Obese ($n = 52$) (%)	p value
Total of postoperative complications[a]	12.2 (11)	27.7 (13)	5.8 (3)	0.008
Readmission and reoperation[b]	7.8 (7)	6.4 (3)	1.9 (1)	0.350
Wound healing problems of the vaginal cuff or cervical stump	7.8 (7)	8.5 (4)	1.9 (1)	0.302
Functional pain and dyspareunia[c]	3.3 (3)	10.6 (5)	1.9 (1)	0.086
Peritoneal adhesions requiring operative revision	5.6 (5)	4.3 (2)	0 (0)	0.234
Intraoperative large vessel injuries	0 (0)	0 (0)	0 (0)	–
Intraoperative bowel injuries	0 (0)	0 (0)	0 (0)	–
Intraoperative urinary tract injuries	0 (0)	0 (0)	0 (0)	–

Total numbers of patients in parentheses. Statistical test used: Chi-square test and Fisher's exact test. The values in the table do not add up because of comorbidities; therefore, each row has to be interpreted separately

BMI body mass index

[a] Includes all ambulatory manageable cases and all readmissions and reoperations

[b] Includes all patients that needed readmission and reoperation, regardless of the underlying complication(s)

[c] Defined as discomfort or pain without demonstrable anatomic findings

Table 2 gives an overview of the postoperative complications. The overall rate of postoperative complications differed significantly between the weight groups ($p = 0.008$). The group of overweight women had the highest proportion of complications and the group of obese

women had the lowest. However, the rate of women who required readmission and reoperation was not elevated in the overweight group. Furthermore, no noticeable variations in the sorts of complications were detected.

Discussion

In this paper, we present data about the impact of the body mass index on laparoscopic hysterectomy for benign disease. The percentage of overweight and obese women in our study population supports the thesis that excess of weight seems to be an increasingly significant challenge. But there is still a debate about the influence of overweight and obesity on peri- and postoperative complications of laparoscopic hysterectomy.

A review about the impact of obesity on women's health found that obesity has a negative influence on the menstrual cycle throughout life [11]. Terry et al. [12] suggested that adiposity is a risk factor for the development of uterine fibroids. However, we neither found any differences between the weight groups with respect to the frequency of the appearance of uterine fibroids or any other medical conditions, nor did we observe elevated frequencies of any concomitant procedures that were necessary in addition to the hysterectomy in obese patients.

To our knowledge, we present the longest follow-up time of all collectives investigated for the same subject. Other authors did not mention their follow-up times or had been observing their patients only for a couple of weeks [7, 8, 13]. However, the postoperative complication rates we reported may be biased by the fact that not all of the women had their follow-up visits at our hospital. It is possible that some postoperative complications were not reported to us, even though all patients had follow-up visits. This is a potential limitation of our study.

The mean age in our patient collective was comparable to the mean ages of other patient groups that were scanned for BMI differences after hysterectomy for benign disease [8, 13]. Mean patient ages tend to be slightly higher when patients with malignant diseases are included in the studies [5–7].

The uterus weights did not differ significantly between the weight groups, but overweight and obese women tended to have larger uteri than patients with normal weight. In spite of the weights of the resected uteri being high in our study, only one laparoconversion had to be performed. Read in conjunction with the high mean BMI of our patients, our laparoconversion rate was remarkably low.

The intraoperative blood loss we report is the lowest we found in the literature about the same subject [5, 7, 14]. However, the blood losses differed significantly between the weight groups. Overweight women had the highest amount of blood loss, followed by obese and normal weight patients. But the differences between the groups were so low that they do not seem to be clinically relevant. It seems that obesity is not a risk factor for bleeding complications during laparoscopic hysterectomy. Mueller et al. [8] even found a tendency toward a lower hemoglobin change in women with a BMI over 30 in a population of 257 women undergoing TLH.

We can confirm the experience of other authors who suggest that the length of the operation increases with the BMI of the patients [5, 13–15]. It is very likely that this is a result of the longer time needed to visualize the structures in the deep pelvis when the amount of peritoneal fat is increased. This may be important for the surgical planning and the higher costs associated with a longer utilization of the operating room. But the operating time seems not to have a relevant impact on the surgical outcomes.

During our study period, no iatrogenic injuries to the bowel, the bladder, the ureters or to the large vessels were observed. Moreover, only one laparotomy had to be performed. Our data shows that intraoperative complication rates can be minimal even when many of the patients are overweight or obese.

The total of postoperative complications differed significantly between the weight groups in our study population. Overweight patients had the highest and obese patients the lowest rate of complications. On closer examination, however, this finding can be put into perspective by the fact that the weight groups did not differ in terms of major complications that led to readmission or reoperation. Moreover, no statistically relevant differences were found with reference to the kinds of complications that we observed. There was just a non-significant tendency toward elevated rates of functional pain and dyspareunia in the group of overweight patients.

We cannot corroborate the thesis that excess of weight has a significant negative effect on laparoscopic hysterectomy. In our study population, the operating time increased with the weight of the patients, but obesity did not influence the occurrence of peri- or postoperative complications. Hence, we think that laparoscopic hysterectomy is a feasible method even in obese and morbidly obese women, and that it is a safe alternative to abdominal or vaginal hysterectomy in the obese.

Conflict of interest The authors indicate no potential conflicts of interest. This study was not funded.

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4.1 Beschreibung des Eigenanteils an Publikation 2

Die Grundidee zur Analyse des Einflusses des Body Mass Index auf intra- und postoperative Komplikationen bei der laparoskopischen Hysterektomie am Universitätsklininikum des Saarlandes stammt von mir selbst und wurde in Zusammenarbeit mit Herrn Priv.-Doz. Dr. med. Ingolf Juhasz-Böss weiterentwickelt. Frau Dr. med. Julia Radosa brachte ebenfalls wichtige Ideen in die Konzeption der Fragestellungen mit ein. Ich selbst habe die Datenerhebung zur Studie in Absprache mit Herrn Priv.-Doz. Dr. med. Ingolf Juhasz-Böss vorgenommen. Die Operationen der Patientinnen wurden zum Großteil von Herrn Professor Dr. med. Erich-Franz Solomayer, Herrn Professor Dr. med. Achim Rody, Herrn Priv.-Doz. Dr. med. Ingolf Juhasz-Böss und Herrn Dr. med. Sascha Baum durchgeführt. Die Auswertung der Daten erfolgte durch Herrn Priv.-Doz. Dr. med. Stefan Gräber in Zusammenarbeit mit mir. Die Manuskripterstellung sowie die Einreichung des Manuskriptes bei Archives of Gynecology and Obstetrics erfolgten durch mich selbst in enger Abstimmung mit Herrn Priv.-Doz. Dr. med. Ingolf Juhasz-Böss. Alle Autoren hatten vor der Einreichung des Manuskriptes die Gelegenheit, den Entwurf zu lesen und Änderungs- sowie Ergänzungsvorschläge zu äußern und machten davon auch Gebrauch.

4.2 Aus Publikation 2 hervorgegangene Kongresspräsentationen

Vorträge

59. Kongress der Deutschen Gesellschaft für Gynäkologie und Geburtshilfe, München, Oktober 2012: „Laparoskopische Hysterektomie: Welche Rolle spielt der Body Mass Index (BMI)? Eine Erfahrungsanalyse an 200 Patientinnen“ (Referent: David Bardens)

Poster

22nd Annual Congress of the European Society of Gynecological Endoscopy (ESGE), Berlin, October 2013: „The impact of the body mass index (BMI) on laparoscopic hysterectomy for benign disease” (Autoren: Bardens D., Solomayer E., Radosa J., Rody A., Baum S., Juhasz-Böss I.)

59. Kongress der Deutschen Gesellschaft für Gynäkologie und Geburtshilfe, München Oktober 2012: „Laparoskopische Hysterektomie: Welchen Rolle spielt der Body Mass Index (BMI)? Eine Erfahrungsanalyse von 200 Fällen“ (Autoren: Bardens D., Solomayer E., Rody A., Baum S., Juhasz-Böss I.)

4.3 Für Publikation 2 erhaltene Auszeichnungen

Das Abstract „The impact of the body mass index (BMI) on laparoscopic hysterectomy for benign disease“ erhielt im Dezember 2013 eine Auszeichnung des European Training Center for Gynecologic Endoscopy (ETC), dotiert mit einem Stipendium in Höhe von 400 €. (Preisträger: David Bardens)

5. Publikation 3: Five minutes of extended assisted ventilation with an open umbilical trocar valve significantly reduces postoperative abdominal and shoulder pain in patients undergoing laparoscopic hysterectomy

Die Arbeit „Five minutes of extended assisted ventilation with an open umbilical trocar valve significantly reduces postoperative abdominal and shoulder pain in patients undergoing laparoscopic hysterectomy.“ ist im November 2013 im European Journal of Obstetrics & Gynecology and Reproductive Biology, herausgegeben von Elsevier Scientific Publishers Ireland Ltd., Irland, erschienen.

Auf den folgenden Seiten findet sich die Arbeit in der veröffentlichten Originalversion.

European Journal of Obstetrics & Gynecology and Reproductive Biology 171 (2013) 122–127

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Five minutes of extended assisted ventilation with an open umbilical trocar valve significantly reduces postoperative abdominal and shoulder pain in patients undergoing laparoscopic hysterectomy

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ABSTRACT

Objective: Residual carbon dioxide contributes substantially to pain following laparoscopic surgery. We evaluated the effects of extended assisted ventilation (EAV) with an open umbilical trocar valve for five additional minutes following laparoscopic hysterectomy on postoperative abdominal and shoulder pain levels. We also examined whether a combination of EAV and trocar site infiltration (TSI) with lidocaine could further reduce postoperative pain levels.

Study design: In this prospective randomized trial, the effectiveness of EAV and EAV/TSI in reducing postoperative abdominal and shoulder pain were compared with that of a standard treatment regime in 283 patients undergoing laparoscopic hysterectomy (total or supracervical). Pain levels were evaluated by self-assessment questionnaire using a numeric rating scale (NRS) and by postoperative piritramid requirement, a surrogate parameter for postoperative analgesic drug requirement. The incidence of nausea and vomiting was also assessed.

Results: Compared with the standard treatment regime, EAV reduced abdominal pain levels significantly at 3 h (NRS score, 3.21 ± 1.56 *vs.* 4.73 ± 1.71) and 24 h (3.82 ± 1.49 *vs.* 4.95 ± 1.68) postoperatively (both $p < 0.01$). EAV also significantly reduced shoulder pain at 24 h (EAV *vs.* control, 4.28 ± 1.51 *vs.* 5.14 ± 1.49) and 48 h (3.64 ± 1.66 *vs.* 4.22 ± 1.43) postoperatively (both $p < 0.01$). Patients in the EAV group had significantly lower piritramid requirements compared with standard treatment at 3 h post-operatively (4.28 ± 2.09 mg *vs.* 6.31 ± 2.21 mg; $p < 0.01$). EAV/TSI showed no additional benefit in terms of pain reduction compared with EAV alone. Incidences of postoperative nausea and vomiting were not reduced by EAV or EAV/TSI.

Conclusion: EAV was found to be an effective and safe method to reduce postoperative pain levels in patients undergoing laparoscopic hysterectomy.

1. Introduction

Laparoscopic procedures reduce surgical trauma, postoperative morbidity, and hospitalization in comparison with conventional approaches *via* laparotomy [1–4]: many gynecological endoscopic interventions for benign pathologies are currently conducted in outpatient settings [5,6]. Patients, however, frequently experience high levels of pain postoperatively, counteracting the benefits of minimally invasive laparoscopic surgery [7]. Pathophysiologically, two factors contribute to post-laparoscopic pain: (1) irritation of intra-abdominal visceral structures by carbon dioxide (CO_2) use during endoscopic intervention and (2) surgical trauma, including abdominal wall incision and iatrogenic intra-abdominal damage [8–11]. In a survey of approximately 6000 laparoscopic procedures, McGrath et al. [12] found that 30% of patients complained of moderate to severe pain 24 h postoperatively.

The aim of this randomized prospective trial was to establish a safe and effective method for residual CO_2 removal at the end of laparoscopic intervention. We evaluated the impact of extended assisted ventilation (EAV), using an open umbilical trocar sleeve

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valve with the patient in the Trendelenburg position, on perceived postoperative pain and analgesic drug requirements. We also investigated whether the combined use of this clinical maneuver and trocar incision site infiltration (TSI) with lidocaine could further reduce postoperative pain levels.

2. Patients and methods

This prospective, randomized, controlled, single-center trial was part of a multidisciplinary research project conducted at Saarland University Hospital, Homburg, Germany, to evaluate surgical outcomes and postoperative quality of life after hysterectomy for benign gynecological conditions. Saarland University Hospital serves as a tertiary university referral center for the federal states of Saarland and Rhineland-Palatinate. The study protocol was approved by the hospital's ethics board and all participants provided written informed consent.

Participants were recruited between July 2009 and December 2012. Inclusion criteria were: (1) age 30–70 years, (2) hysterectomy indicated for a benign gynecological condition, and (3) American Society of Anesthesiologists physical status classification of I–II. Exclusion criteria were: (1) refusal to participate in the study, (2) severe intraoperative complication(s), defined as bowel, bladder, or ureter injury, major bleeding requiring intraoperative or postoperative transfusion, and/or pronounced subcutaneous emphysema;(3) unintended conversion from laparoscopy to laparotomy or abandonment of the intended surgical procedure; (4) lack of 48-h postoperative follow up; and (5) inability to obtain postoperative data due to postoperative Clavien-Dindo grade III-V post-operative complications (Table 1).

Using Fisher's *F* distribution [13], we determined that a sample of 86 patients per study group was required for an estimated effect size of 0.5 on the numeric rating scale (NRS) for 24-h postoperative abdominal and shoulder pain and a type II error (β) of 0.2, with a Bonferroni-adjusted significance level of 0.01 (alpha). In anticipation of study drop-outs for surgical reasons, we used an as-treated analytical design. All study participants were assigned randomly to study groups (control, EAV, EAV/TSI) using a computer-generated randomization list. The suitability of collected data for analysis was assessed monthly, and trial enrollment was continued until the minimum of 86 patients per group with suitable data was obtained.

Preoperatively, all patients underwent gynecological examination and transvaginal ultrasound. Basic laboratory tests, including the measurement of preoperative hemoglobin concentrations, were performed.

All surgeries were performed in the hospital's Department of Gynecology. Laparoscopic hysterectomy was performed using four ports: one 10-mm optic trocar inserted through the umbilicus; two 3-mm working trocars inserted through the inferolateral abdominal wall, two fingers' distance above the iliac crest; and one 3-mm working trocar in the suprapubic area, two fingers' distance above the symphysis pubis. CO_2, the distention medium, was insufflated through the Veress needle at 20 mm Hg pressure until placement of all four ports was complete. Thereafter, the procedure was continued under 14 mm Hg pressure with a CO_2 flow rate $\leq$3 L/min. Detailed descriptions of the surgical techniques used for total laparoscopic hysterectomy (TLH) and laparoscopic supracervical hysterectomy (LASH) in this study can be found elsewhere [14,15]. At the end of the procedure, an intra-abdominal drain (French 18 gauge) was placed through one of the 3-mm iliac trocars for postoperative monitoring. Patients were then treated according to group protocols.

In the control group, the remaining two 3-mm working trocars were removed under visual control. The umbilical optic trocar valve was opened, the abdominal wall was compressed to remove

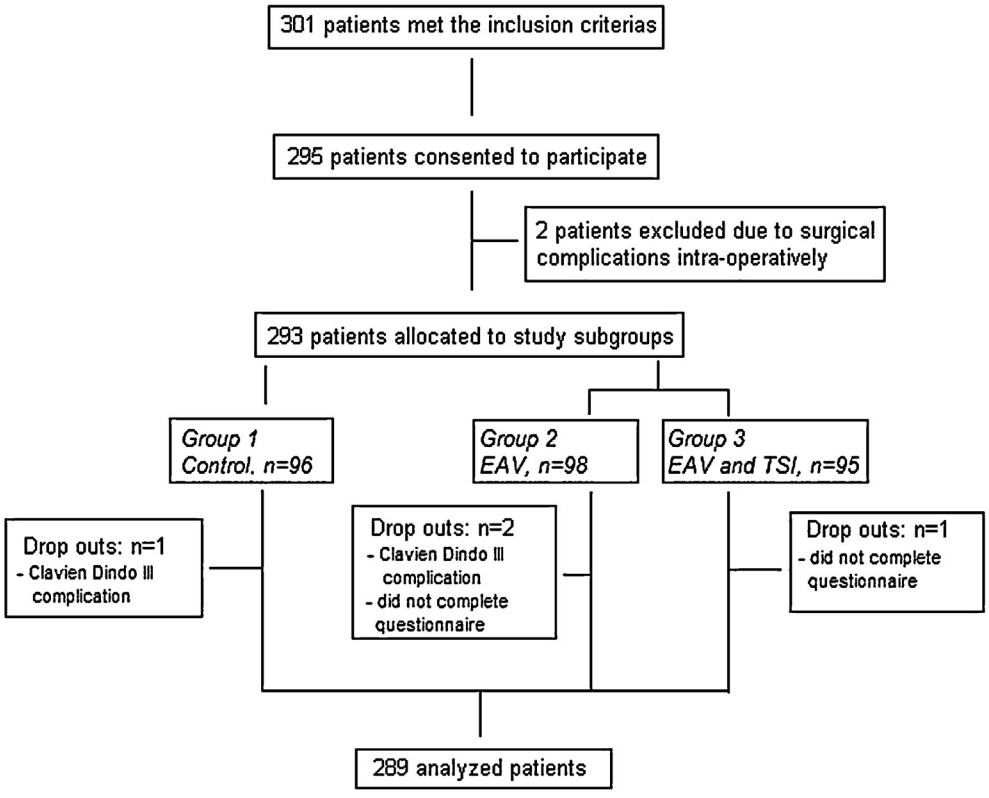

Fig. 1. EAV: extended assisted ventilation; TSI: trocar site infilteration.

Table 1
Patients' characteristics and surgical outcome.

	All patients		Group 1 Control		Group 2 EAV		Group 3 EAV and TSI		
	$n=289$		$n=96$		$n=98$		$n=95$		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*p* value
Age (years)	45.44	7.55	45.21	6.38	45.74	8.35	45.41	7.93	*0.21*
BMI (kg/m^2)	26.72	6.1	26.18	5.82	27.14	6.11	27.72	6.32	*0.43*
	N		*N*		*N*		*N*		
Type of surgery									
TLH	184		61		59		64		
LASH	105		33		37		35		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Duration of surgery (min.)	139.31	56.42	136.27	57.6	131.23	49.14	151.18	60.31	*0.07*
Total CO_2 Volume (l)	320.48	98.22	319.72	94.41	331.41	95.89	310.11	100.7	*0.83*
Estimated blood loss intra-operatively (ml)	92.87	87.22	93.41	82.1	89.5	78.23	96.23	98.72	*0.91*
postoperative complication	*N*		*N*		*N*		*N*		
Clavien-Dindo Grade IV-V	0		0		0		0		
Clavien-Dindo Grade III	2		1		1		0		
Clavien-Dindo Grade I-II	14		4		6		4		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Postoperative hospitalization (days)			5.93	1.72	5.38	1.21	5.32	1.41	*0.11*

Abbreviations: EAV, extended assisted ventilation; TSI, trocar site infiltration; TLH, total laparoscopic hysterectomy; LASH, laparoscopic supracervical hysterectomy.

residual CO_2, and the optic trocar was removed under visual control. In the EAV and EAV/TSI groups, the umbilical valve was left open after working trocar removal and abdominal compression. The patient was placed in an anti-Trendelenburg position and received assisted ventilation for an additional 5 min. Ventilation was pressure controlled (positive end-expiratory pressure, 3–5 mm Hg; maximum inspiratory pressure, 25 mm Hg) and respiratory volume was regulated (end-expiratory CO_2 target, 30–40 mm Hg). The patient was then moved to a horizontal position and the umbilical optic trocar was removed under visual control. Additionally, in the EAV/TSI group, the umbilical and working trocar incisions were each infiltrated with 5 mL 0.4% lidocaine hydrochloride (Xylocaine; Astra-Zeneca, Wedel, Germany) after optic trocar removal. In all groups, the port incisions were closed with 3-0 moncryl sutures (Monocryl Plus 3-0; Ethicon, Norderstedt, Germany) using a standardized single-knot technique.

All patients received perioperative antibiotics and had an indwelling urinary catheter until the first postoperative morning. Low molecular weight heparin was administered as thromboembolism prophylaxis. All patients received intravenous metamizole (Novaminsulfon, 1 g/2 mL; Ratiopharm, Neu-Ulm, Germany) diluted in 100 ml 0.9% sodium chloride every 6 h on the day of surgery and first postoperative day, with the first dose given 60 min after arrival in the postanesthesia care unit. Upon request, 7.5 mg piritramid (Dipidolor; Jansen-Cilag, Neuss, Germany) was administered intravenously every 6 h for additional postoperative pain management. Mean postoperative piritramid requirements (in milligrams per patient) at 3 and 24 h postoperatively were used as surrogate parameters of postoperative analgesic drug requirements in each group.

At-rest abdominal and shoulder pain levels were evaluated 3, 24, and 48 h postoperatively using a standardized NRS (range, 0–10). Patients were also asked about the occurrence of nausea and/or vomiting. The duration of surgery (from trocar placement to closure of all trocar sites or TSI completion), total volume of CO_2 delivered, duration of postoperative hospitalization (first postoperative day to day of discharge), and postoperative complications (Clavien-Dindo classification [16]: major, grades III–V; minor, grades I–II) were documented.

Data were collected in an Excel database (Microsoft Corporation, Redmond, WA, USA). Student's *t*-test and Fisher's exact test with Bonferroni correction were used for comparisons between the control and interventional groups. A p value ≤ 0.01 was considered to indicate statistical significance. All statistical calculations were conducted with GraphPad QuickCalcs software (La Jolla, CA, USA). Results are reported as means ± standard deviations.

3. Results

Of 301 eligible patients scheduled for laparoscopic hysterectomy (TLH or LASH) during the study period, 295 women agreed to participate in this trial. Two patients were excluded due to intraoperative conversion from laparoscopy to laparotomy. The remaining 293 patients were allocated to the three study groups. Four patients did not complete the postoperative questionnaire due to a post-operative haematoma with subsequent surgical revision (Clavien-Dindo grade III) ($n=2$) or discharge from the hospital within 24 h postoperatively ($n=2$). Thus, analyses included a total of 289 patients: 96 in the control group, 98 in the EAV group, and 95 patients in the EAV/TSI group (Fig. 1).

The mean age of the study cohort was 45.4 years and the mean body mass index was 27 kg/m^2. One hundred and eight-four patients underwent TLH and 105 underwent LASH. Mean intraoperative blood loss was 93.1 mL and a mean of 320.6 mL CO_2 was insufflated during surgery. Two Clavien-Dindo grade III and 14 grade I and II postoperative complications occurred, and the mean duration of hospitalization was 5.5 ± 14 days. These parameters did not differ significantly among groups (Table 1).

The mean duration of surgery was longer in the EAV/TSI group (151.2 min) than in the control (139.6 min) and EAV (131.2 min) groups, but this difference was not significant ($p = 0.07$). Thus, EAV and/or TSI did not prolong surgical time.

In the control group, mean NRS scores for abdominal pain were 4.73, 4.95, and 3.62 at 3, 24, and 48 h postoperatively, respectively. Abdominal pain levels were significantly lower in both interventional groups than in the control group at 3 and 24 h postoperatively (EAV group: 3.21 at 3 h, 3.82 at 24 h; $p < 0.01$ and EAV/TSI group: 3.04 at 3 h, 3.62 at 24 h; $p = 0.01$). Comparison of abdominal pain scores in the EAV and EAV/TSI groups showed no additional pain reduction benefit of TSI.

Mean postoperative NRS scores for shoulder pain at 24 and 48 h were significantly lower in the EAV group (4.28 and 3.64) than in

the control group (5.14 and 4.22; $p < 0.01$). Mean scores were significantly lower in the EAV/TSI group at 24 h (4.15; $p < 0.01$). No significant difference in shoulder pain at 3 h postoperatively was observed among groups. EAV/TSI did not reduce shoulder pain significantly in comparison with EAV alone.

Mean postoperative piritramid requirements at 3 h were significantly lower in the EAV (4.28 mg) and EAV/TSI (4.05 mg) groups than in the control group (6.31 mg; $p \leq 0.01$). At 24 h, piritramid requirements remained lower in the EAV (2.87 mg) and EAV/TSI (2.91 mg) groups than in the control group (3.71 mg), but these differences were not significant ($p > 0.05$). No significant difference in this parameter was observed between the EAV and EAV/TSI groups (Table 2). The overall incidence of nausea was 33.2% at 3 h postoperatively and 16.61% at 24 h postoperatively; that of vomiting was 11.1% and 2.77%, respectively. No significant difference in these parameters was observed among groups (Table 3).

4. Comment

In this study, we evaluated the effects of residual CO_2 removal and TSI at the end of laparoscopic surgery on postoperative pain reduction. Previous studies have consistently demonstrated the contribution of CO_2 to postoperative pain [17–19], but the pathophysiological pathways involved remain unclear. Some authors have hypothesized that CO_2 acts as a peritoneal irritant, inducing morphological and biochemical changes in the mesothelial surface that cause pain [19,20]. CO_2 is also thought to directly irritate the phrenic nerve, referring the pain to C4 that is perceived clinically as shoulder pain; this epiphenomenon occurs in up to 80% of patients following laparoscopy [21,17]. Jackson and colleagues [22] demonstrated a direct correlation between the amount of residual CO_2 and the intensity of pain after laparoscopic procedures.

Several techniques have been introduced to reduce residual intra-abdominal CO_2 or neutralize its effect on visceral structures. Fredman et al. [23] found that residual CO_2 removal by active aspiration and manual compression of the abdominal wall at the end of laparoscopic intervention reduced postoperative analgesic drug requirements. CO_2 removal by saline irrigation in the right subdiaphragmatic space reduced postoperative shoulder pain following laparoscopic surgery [24]. Recently, Phelps et al. [25] described the use of repetitive pulmonary recruitment maneuvers with brief intrapulmonary pressure peaks (to 60 mm Hg) to remove residual CO_2 through the open sleeve valve at the end of laparoscopic surgery; this technique significantly reduced postoperative pain and nausea. External studies have validated the effectiveness of this simple clinical maneuver for postoperative pain management, and some endoscopic centers have implemented it in routine clinical practice [26,27]. This method, however, may cause iatrogenic barotrauma and subsequent pneumothorax [25,28].

In the present study, we modified Phelps' technique to avoid increased airway pressure by replacing the pulmonary recruitment maneuvers with EAV in an anti-Trendelenburg position (30°) with an open trocar valve and simultaneous manual compression of the abdominal wall for 5 min at the end of the laparoscopic procedure. The observed reduction in postoperative pain, reflected in patients' self-assessments and reduced piritramid requirements, was comparable to the results of previous studies employing CO_2 removal techniques that increased airway pressure [25,26]. This finding suggests that 5 min of EAV with physiological pressures of 15–25 mm Hg effectively eliminates residual CO_2.

Although our method did not significantly prolong surgery in this study, the potential increase in operative time might be a clinically relevant factor in endoscopic centers where short laparoscopic interventions are performed successively. A shorter period of auxiliary respiration might be equally effective; a

Table 2
Main measurement outcomes.

Post-operative Pain									
	Group 1		Group 2		Group 3		p value		
	Control ($n=96$)		EAV ($n=98$)		EAV and TSI ($n=95$)		Control vs EAV	Control vs EAV and TSI	EAV vs. EAV and TSI
	Mean	SD	Mean	SD	Mean	SD			
Abdominal pain (NRS Score/pts)									
3 h po	4.73	1.71	3.21	1.56	3.04	1.44	*<0.01*	*<0.01*	0.43
24 h po	4.95	1.68	3.82	1.49	3.62	1.79	*<0.01*	*<0.01*	0.45
48 h po	3.62	1.44	3.04	1.62	2.82	1.45	0.09	0.04	0.32
Shoulder pain (NRS Score/pts)									
3 h po	2.23	1.52	2.18	1.39	2.52	1.38	0.29	0.17	0.09
24 h po	5.14	1.49	4.28	1.51	4.15	1.48	*<0.01*	*<0.01*	0.55
48 h po	4.22	1.43	3.64	1.66	3.72	1.64	*<0.01*	0.03	
Piritramid requirement (mg)									
3 h po	6.31	2.21	4.28	2.09	4.05	2.01	*<0.01*	*<0.01*	0.44
24 h po	3.71	2.32	2.87	1.23	2.91	1.41	0.03	0.04	0.83
Post-operative nausea and vomiting									
	N		*N*		*N*				
Nausea									
3 h po	32		29		35		0.99	0.41	0.28
24 h po	18		16		14		0.78	0.9	0.51
Vomitting									
3 h po	13		10		9		0.14	0.67	0.99
24 h po	2		2		4		0.99	0.8	0.37

Abbrevation: EAV, extended assisted ventilation; TSI, trocar site infiltration; NRS score, numeric rating scale score; po, post-operatively.

time-response study to determine the minimum effective duration of EAV should be conducted.

TSI with a local anesthetic is another commonly used strategy to reduce post-laparoscopic pain [29]. In laparotomy, wound margins are infiltrated postoperatively – and sometimes preoperatively – with lidocaine [30,31]. Because the introduction of the camera and working trocars in laparoscopy entails much less surgical trauma compared with conventional access in laparotomy, the benefits of anesthetic infiltration for postoperative pain management are not comparable between techniques [29,32]. In our study, TSI with lidocaine did not significantly reduce postoperative pain, measured by patients' self-assessments and piritramid requirements, compared with EAV alone. Previous evaluations of the clinical use of lidocaine in wound incisions or intraperitoneally in laparoscopic procedures have produced inconsistent results: some authors found significant reductions in postoperative pain, but others could not reproduce these results [33,34]. Given the short half-life of lidocaine (~60 min in plasma), bupivacaine (half-life in plasma, 180 min) might be more suitable for TSI [29,35], but the results of studies using bupivacaine for postoperative pain management have also been variable [36,37]. Some groups have examined extended intraperitoneal administration of local anesthetics, most commonly lidocaine and bupivacaine, in laparoscopic surgery. The anesthetic is administered to the intra-abdominal surgical site to create a visceral block, thereby reducing postoperative pain [32].

The comparability of these anesthetic strategies for laparoscopic surgery is limited by considerable variation in anesthetic type, dosage, application mode (TSI *vs.* TSI and intraperitoneal application), and timing (postoperative *vs.* preoperative + postoperative). A systematic meta-analysis of the clinical use of local anesthetics in laparoscopic surgery found that TSI had no significant effect on pain reduction; additional intra-abdominal application appeared to reduce pain, but the authors questioned the clinical impact of this effect [29].

The risks associated with the use of local anesthetics for pain reduction in laparoscopic surgery must be weighed against their potentially limited benefits. Especially after intraperitoneal application, toxic plasma levels of local anesthetics have been occasionally observed [34,38]. In France, severe adverse effects following drug administration are centrally registered in a pharmacovigilance database. From 1995 to 2006, 0.3% of all reported incidents ($n = 731$), including eight fatalities, occurred after the application of local anesthetics; in the majority (71.4%) of cases, lidocaine or bupivacaine caused neurological (22.1%), cardiovascular (15.3%), or anaphylactic reactions (19.4%) [39].

In conclusion, 5 min of postoperative EAV with simultaneous manual compression of the abdominal wall to remove residual CO_2 is a simple and effective maneuver that was found to reduce post-laparoscopic pain. Additional TSI with lidocaine had no further beneficial impact on postoperative pain. In combination with previously reported results and within the context of potentially severe side effects, we therefore caution against the routine use of TSI in laparoscopic interventions.

Conflict of interest statement

All authors declare no conflict of interest.

Role of the funding source

No study sponsors have been involved.

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5.1 Beschreibung des Eigenanteils an Publikation 3

Die Grundidee zur Durchführung der Studie zur Verringerung der postoperativen Schmerzen nach laparoskopischer Hysterektomie am Universitätsklininikum des Saarlandes stammt von Herrn Dr. med. Sascha Baum. Die Datenerhebung im Bezug auf die Anamnese der Patientinnen und die operativen Daten erfolgte durch mich und Frau Dr. med Julia Radosa. Die Datenerhebung im Bezug auf die Schmerzfragebögen und den postoperativen Schmerzmittelverbrauch erfolgte durch Frau Daniela Guzman-Castro. Frau Dr. med. Kathrin Brün aus der Abteilung für Anästhesiologie und Intensivmedizin betreute das Projekt von anästhesiologischer Seite und war verantwortlich für die Durchführung der Nachbeatmungen. Die Operationen der Patientinnen wurden von Herrn Professor Dr. med. Erich-Franz Solomayer, Herrn Professor Dr. med. Achim Rody, Herrn Priv.-Doz. Dr. med. Ingolf Juhasz-Böss und Herrn Dr. med. Sascha Baum durchgeführt. Die Auswertung der Daten erfolgte durch Frau Dr. med. Julia Radosa in Zusammenarbeit mit Herrn Dr. med. Marc P. Radosa und Frau Dr. med. Russalina Mavrova. Die Manuskripterstellung erfolgte durch Frau Dr. med. Julia Radosa und Herrn Dr. med. Marc P. Radosa unter Supervision durch Herrn Dr. med. Sascha Baum. Die Einreichung des Manuskriptes beim European Journal of Obstetrics & Gynecology and Reproductive Biology erfolgte durch Frau Dr. med. Julia Radosa. Alle Autoren hatten vor der Einreichung des Manuskriptes die Gelegenheit, den Entwurf zu lesen und Änderungs- sowie Ergänzungsvorschläge zu äußern und machten davon auch Gebrauch.

5.1 Aus Publikation 3 hervorgegangene Kongresspräsentationen

Vorträge und Poster

Bisher wurde die Arbeit noch nicht auf Kongressen präsentiert.

6. Literaturverzeichnis

Das folgende Literaturverzeichnis bezieht sich lediglich auf die erweiterte Zusammenfassung.

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7. Lebenslauf

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