LIST OF PUBLICATIONS

In REVERSE CHRONOLOGICAL ORDER

PEER REVIEWED JOURNALS

Original articles published

Authors (*)	Arezzo, Alberto; Balague, Carmen; Targarona, Eduardo; Borghi, Felice; Giraudo, Giorgio; Ghezzo, Luigi; Arroyo, Antonio; Sola-Vera, Javier; De Paolis, Paolo; Bossotti, Maurizio; Bannone, Elisa; Forcignanò, Edoardo; Bonino, Marco Augusto; Passera, Roberto; Morino, Mario
Title	Colonic stenting as a bridge to surgery versus emergency surgery for malignant colonic obstruction: results of a multicentre randomised controlled trial (ESCO trial)
Journal	SURGICAL ENDOSCOPY
Year of publication	2017
Volume	31
pages	3297
	3305
WOS Impact factor	3.747
Type of publication	Original Article
Authors	Penna, Marta; Hompes, Roel; Arnold, Steve; Wynn, Greg; Austin, Ralph; Warusavitarne, Janindra; Moran, Brendan; Hanna, George B.; Mortensen, Neil J.; Tekkis, Paris P.; Arezzo, Alberto; Morino, Mario
Title	Transanal Total Mesorectal Excision: International Registry Results of the First 720 Cases
Journal	ANNALS OF SURGERY
Year of publication	2017
Volume	266
pages	111
	117
WOS Impact factor	8.98
Type of publication	Original Article
Authors	Francis, Nader; Penna, Marta; Mackenzie, Hugh; Carter, Fiona; Hompes, Roel

Title	Consensus on structured training curriculum for transanal total mesorectal excision (TaTME)
Journal	SURGICAL ENDOSCOPY
Year of publication	2017
Volume	31
pages	2711
	2719
WOS Impact factor	3.747
Type of publication	Original Article
Authors	Garbarini, Aldo; Reggio, Dario; Arolfo, Simone; Bruno, Marco; Passera, Roberto; Catalano, Giorgia; Barletti, Claudio; Salizzoni, Mauro; Morino, Mario; Petruzzelli, Luca; Arezzo, Alberto
Title	Cost analysis of laparoendoscopic rendezvous versus preoperative ERCP and laparoscopic cholecystectomy in the management of cholecystocholedocholithiasis
Journal	SURGICAL ENDOSCOPY
Year of publication	2017
Volume	31
pages	3291
	3296
WOS Impact factor	3.747
Type of publication	Original Article
Authors	Agresta, Ferdinando; Campanile, Fabio Cesare; Podda, Mauro; Cillara, Nicola; Pernazza, Graziano; Giaccaglia, Valentina; Ciccoritti, Luigi; Ioia, Giovanna; Mandalà, Stefano; la Barbera, Camillo; Birindelli, Arianna; Sartelli, Massimo; Di Saverio, Salomone; Anania, Gabriele; Vettoretto, Nereo; Arezzo, Alberto; Campli, Mario; Bergamini, Carlo; Carlucci, Michele; Zago, Mauro; Mirabella, Antonino; Lupo, Massimo; Piccoli, Micaela; Ansaloni, Luca; Cocorullo, Gianfranco; Baiocchi, Luca; Allaix, Marco; Saia, Mario; Luridiana, Gianluigi
Title	Current status of laparoscopy for acute abdomen in Italy: a critical appraisal of 2012 clinical guidelines from two consecutive nationwide surveys with analysis of 271,323 cases over 5 years
Journal	SURGICAL ENDOSCOPY
Year of publication	2017

Volume	31
pages	1785
	1795
WOS Impact factor	3.747
Type of publication	Original Article
Authors (*)	Arezzo, Alberto; Passera, Roberto; Bullano, Alberto; Mintz, Yoav; Kedar, Asaf; Boni, Luigi; Cassinotti, Elisa; Rosati, Riccardo; Fumagalli Romario, Uberto; Sorrentino, Mario; Brizzolari, Marco; Di Lorenzo, Nicola; Gaspari, Achille Lucio; Andreone, Dario; De Stefani, Elena; Navarra, Giuseppe; Lazzara, Salvatore; Degiuli, Maurizio; Shishin, Kirill; Khatkov, Igor; Kazakov, Ivan; Schrittwieser, Rudolf; Carus, Thomas; Corradi, Alessio; Sitzman, Guenther; Lacy, Antonio; Uranues, Selman; Szold, Amir; Morino, Mario
Title	Multi-port versus single-port cholecystectomy: results of a multi-centre, randomised controlled trial (MUSIC trial)
Journal	SURGICAL ENDOSCOPY
Year of publication	2017
Volume	31
pages	2872
	2880
WOS Impact factor	3.747
Type of publication	Original Article
Authors	Bernth, Julius E.; Arezzo, Alberto; Liu, Hongbin
Title	A Novel Robotic Meshworm With Segment-Bending Anchoring for Colonoscopy
Journal	IEEE ROBOTICS AND AUTOMATION LETTERS
Year of publication	2017
Volume	2
pages	1718
	1724
WOS Impact factor	
Type of publication	Original Article
Authors	Faletti, Riccardo; Gatti, Marco; Arezzo, Alberto; Stola, Silvia; Benedini, Maria C; Bergamasco, Laura; Morino, Mario; Fonio, Paolo

Title	Preoperative staging of Rectal Cancer using Magnetic Resonance Imaging: comparison with pathological staging
Journal	MINERVA CHIRURGICA
Year of publication	2017
Volume	Epub ahead of print
pages	1
	12
WOS Impact factor	1.115
Type of publication	Original Article
Authors	Guanà, Riccardo; Ferrero, Luisa; Garofalo, Salvatore; Cerrina, Alessia; Cussa, Davide; Arezzo, Alberto; Schleef, Jurgen
Title	Skills Comparison in Pediatric Residents Using a 2-Dimensional versus a 3-Dimensional High-Definition Camera in a Pediatric Laparoscopic Simulator
Journal	JOURNAL OF SURGICAL EDUCATION
Year of publication	2017
Volume	74
pages	644
	649
WOS Impact factor	2.163
Type of publication	Original Article
Authors	Arezzo, Alberto; Mintz, Yoav; Allaix, Marco Ettore; Arolfo, Simone; Bonino, Marco; Gerboni, Giada; Brancadoro, Margherita; Cianchetti, Matteo; Menciassi, Arianna; Wurdemann, Helge; Noh, Yohan; Althoefer, Kaspar; Fras, Jan; Glowka, Jakob; Nawrat, Zbigniew; Cassidy, Gavin; Walker, Rich; Morino, Mario
Title	Total mesorectal excision using a soft and flexible robotic arm: a feasibility study in cadaver models
Journal	SURGICAL ENDOSCOPY
Year of publication	2017
Volume	31
pages	264
	273
WOS Impact factor	3.747

Type of publication	Original Article
Authors	Allaix, Marco E; Giraudo, Giuseppe; Ferrarese, Alessia; Arezzo, Alberto; Rebecchi, Fabrizio; Morino, Mario
Title	10-Year Oncologic Outcomes After Laparoscopic or Open Total Mesorectal Excision for Rectal Cancer
Journal	WORLD JOURNAL OF SURGERY
Year of publication	2016
Volume	40
pages	3052
	3062
WOS Impact factor	2.673
Type of publication	Original Article
Authors	Allaix, Marco E; Furnée, Edgar J B; Mistrangelo, Massimiliano; Arezzo, Alberto; Morino, Mario
Title	Conversion of laparoscopic colorectal resection for cancer: What is the impact on short-term outcomes and survival?
Journal	WORLD JOURNAL OF GASTROENTEROLOGY
Year of publication	2016
Volume	22
pages	8304
	8313
WOS Impact factor	3.365
Type of publication	Original Article
Authors	Alberto Arezzo; Valeria Farina; Caterina Foppa; Laura Gavagna; Mario Morino; Sandro Pasquali; Francesco Pata; Gianluca Pellino; Michele Rubbini; Francesco Selvaggi; Bruno Sensi; Giuseppe Sica; Nepogodiev, Dmitri; - Collaborative, Eurosurg
Title	EuroSurg: a new European student-driven research network in surgery
Journal	COLORECTAL DISEASE
Year of publication	2016
Volume	18
pages	214

	215
WOS Impact factor	2.689
Type of publication	Original Article
Authors	Allaix, Marco Ettore; Arezzo, Alberto; Giraudo, Giuseppe; Arolfo, Simone; Mistrangelo, Massimiliano; Morino, Mario
Title	The Thunderbeat and Other Energy Devices in Laparoscopic Colorectal Resections: Analysis of Outcomes and Costs
Journal	JOURNAL OF LAPAROENDOSCOPIC & ADVANCED SURGICAL TECHNIQUES.
Year of publication	2016
Volume	
pages	1
	5
WOS Impact factor	1.255
Type of publication	Original Article
Authors	Arezzo, A
Title	To TEM or not to TEM: past, present and probable future perspectives of the transanal endoscopic microsurgery platform
Journal	TECHNIQUES IN COLOPROCTOLOGY
Year of publication	2016
Volume	20
pages	271
	272
WOS Impact factor	2.342
Type of publication	Original Article
Authors	Arezzo, A; Cortese, G; Arolfo, S; Bullano, A; Passera, R; Galietti, E; Morino, M
Title	Transanal Endoscopic Operation under spinal anaesthesia
Journal	BRITISH JOURNAL OF SURGERY
Year of publication	2016
Volume	103
pages	916

	920
WOS Impact factor	5.899
Type of publication	Original Article
Authors	Arezzo, Alberto; Arolfo, Simone; Allaix, Marco Ettore; Bullano, Alberto; Miegge, Alice; Marola, Silvia; Morino, Mario
Title	Transanal endoscopic microsurgery for giant circumferential rectal adenomas
Journal	COLORECTAL DISEASE
Year of publication	2016
Volume	18
pages	897
	902
WOS Impact factor	2.689
Type of publication	Original Article
Authors	Ranzani, Tommaso; Ciuti, Gastone; Tortora, Giuseppe; Arezzo, Alberto; Arolfo, Simone; Morino, Mario; Menciassi, Arianna
Title	A Novel Device for Measuring Forces in Endoluminal Procedures
Journal	INTERNATIONAL JOURNAL OF ADVANCED ROBOTIC SYSTEMS
Year of publication	2015
Volume	12
pages	1
	10
WOS Impact factor	615
Type of publication	Original Article
Authors	Yahya Elsayed;Constantina Lekakou;Tommaso Ranzani;Matteo Cianchetti;Mario Morino;Alberto Arezzo;Arianna Menciassi;Tao Geng;CHAKRAVARTHINI M. Saaj
Title	Crimped braided sleeves for soft, actuating arm in robotic abdominal surgery
Journal	MINIMALLY INVASIVE THERAPY & ALLIED TECHNOLOGIES
Year of publication	2015
Volume	24
pages	204

	210
WOS Impact factor	1.279
Type of publication	Original Article
Authors	Gralnek, Ian M; Dumonceau, Jean-Marc; Kuipers, Ernst J; Lanas, Angel; Sanders, David S; Kurien, Matthew; Rotondano, Gianluca; Hucl, Tomas; Dinis-Ribeiro, Mario; Marmo, Riccardo; Racz, Istvan; Arezzo, Alberto; Hoffmann, Ralf-Thorsten; Lesur, Gilles; de Franchis, Roberto; Aabakken, Lars; Veitch, Andrew; Radaelli, Franco; Salgueiro, Paulo; Cardoso, Ricardo; Maia, Luís; Zullo, Angelo; Cipolletta, Livio; Hassan, Cesare
Title	Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline
Journal	ENDOSCOPY
Year of publication	2015
Volume	47
pages	a1
	a46
WOS Impact factor	5.634
Type of publication	Original Article
Authors	Marco E. Allaix;Giuseppe Giraudo;Massimiliano Mistrangelo;Alberto Arezzo;Mario Morino
Title	Laparoscopic versus open resection for colon cancer: 10-year outcomes of a prospective clinical trial
Journal	SURGICAL ENDOSCOPY
Year of publication	2015
Volume	29
pages	916
	924
WOS Impact factor	3.54
Type of publication	Original Article
Authors	Bianco, F; Arezzo, A; Agresta, F; Coco, C; Faletti, R; Krivocapic, Z; Rotondano, G; Santoro, G A; Vettoretto, N; De Franciscis, S; Belli, A; Romano, G M
Title	Practice parameters for early colon cancer management: Italian Society of Colorectal Surgery (Società Italiana di Chirurgia Colo-Rettale; SICCR) guidelines

Journal	TECHNIQUES IN COLOPROCTOLOGY
Year of publication	2015
Volume	19
pages	577
	585
WOS Impact factor	2.32
Type of publication	Original Article
Authors	Arezzo, A; Bianco, F; Agresta, F; Coco, C; Faletti, R; Krivocapic, Z; Rotondano, G; Santoro, G A; Vettoretto, N; De Franciscis, S; Belli, A; Romano, G M
Title	Practice parameters for early rectal cancer management: Italian Society of Colorectal Surgery (Società Italiana di Chirurgia Colo-Rettale; SICCR) guidelines
Journal	TECHNIQUES IN COLOPROCTOLOGY
Year of publication	2015
Volume	19
pages	587
	593
WOS Impact factor	2.32
Type of publication	Original Article
Authors	Alberto Arezzo;Simone Arolfo;Marco Ettore Allaix;Fernando Munoz;Paola Cassoni;Chiara Monagheddu;Umberto Ricardi;Giovannino Ciccone;Mario Morino
Title	Results of Neoadjuvant Short-Course Radiation Therapy Followed by Transanal Endoscopic Microsurgery for T1-T2 N0 Extraperitoneal Rectal Cancer
Journal	INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS
Year of publication	2015
Volume	92
pages	299
	306
WOS Impact factor	4.495
Type of publication	Original Article

Authors	Jose G. Trevino;Rebecca Senetta;Eleonora Duregon;Cristina Sonetto;Rossella Spadi;Massimiliano Mistrangelo;Patrizia Racca;Luigi Chiusa;Fernando H. Munoz;Umberto Ricardi;Alberto Arezzo;Adele Cassenti;Isabella Castellano;Mauro Papotti;Mario Morino;Mauro Risio;Paola Cassoni
Title	YKL-40/c-Met Expression in Rectal Cancer Biopsies Predicts Tumor Regression following Neoadjuvant Chemoradiotherapy: A Multi-Institutional Study
Journal	PLOS ONE
Year of publication	2015
Volume	10
pages	1
	17
WOS Impact factor	3.057
Type of publication	Original Article

Authors	Lorenzo Fuccio;Loredana Correale;Alberto Arezzo;Alessandro Repici;Gianpiero Manes;Cristina Trovato;Benedetto Mangiavillano;Mauro Manno;Claudio Camillo Cortelezzi;Marco Dinelli;Vincenzo Cennamo;Mario de Bellis
Title	Influence of K-ras status and anti-tumour treatments on complications due to colorectal self-expandable metallic stents: A retrospective multicentre study
Journal	DIGESTIVE AND LIVER DISEASE
Year of publication	2014
Volume	46
pages	561
	567
WOS Impact factor	2.963
Type of publication	Original Article

Authors	Yamile Haito-Chavez;Joanna K. Law;Thomas Kratt;Alberto Arezzo;Mauro Verra;Mario Morino;Reem Z. Sharaiha;Jan-Werner Poley;Michel Kahaleh;Christopher C. Thompson;Michele B. Ryan;Neel Choksi;B. Joseph Elmunzer;Sonia Gosain;Eric M. Goldberg;Rani J. Modayil;Stavros N. Stavropoulos;Drew B. Schembre;Christopher J. DiMaio;Vinay Chandrasekhara;Muhammad K. Hasan;Shyam Varadarajulu;Robert Hawes;Victoria Gomez;Timothy A. Woodward;Sergio Rubel-Cohen;Fernando Fluxa;Frank P. Vleggaar;Venkata S. Akshintala;Gottumukkala S. Raju;Mouen A. Khashab

Title	International multicenter experience with an over-the-scope clipping device for endoscopic management of GI defects (with video)
Journal	GASTROINTESTINAL ENDOSCOPY
Year of publication	2014
Volume	80
pages	610
	622
WOS Impact factor	5.369
Type of publication	Original Article
Authors	Roberto Rimonda;Alberto Arezzo;Mario Morino
Title	Reply to: doi: 10.1007/s00464-013-3111-4: TEM or TAMIS: what is the future of transanal endoscopic surgery?
Journal	SURGICAL ENDOSCOPY
Year of publication	2014
Volume	28
pages	1376
	1377
WOS Impact factor	3.256
Type of publication	Original Article
Authors	Simone Arolfo;Marco Ettore Allaix;Marco Migliore;Francesca Cravero;Alberto Arezzo;Mario Morino
Title	Transanal endoscopic microsurgery after endoscopic resection of malignant rectal polyps: a useful technique for indication to radical treatment
Journal	SURGICAL ENDOSCOPY
Year of publication	2014
Volume	28
pages	1136
	1140
WOS Impact factor	3.256
Type of publication	Original Article

Authors	Alberto Arezzo;Simone Arolfo;Massimiliano Mistrangelo;Baudolino Mussa;Paola Cassoni;Mario Morino
Title	Transrectal sentinel lymph node biopsy for early rectal cancer during transanal endoscopic microsurgery
Journal	MINIMALLY INVASIVE THERAPY & ALLIED TECHNOLOGIES
Year of publication	2014
Volume	23
pages	17
	20
WOS Impact factor	1.271
Type of publication	Original Article

Authors	Marco Ettore Allaix;Maurizio Degiuli;Alberto Arezzo;Simone Arolfo;Mario Morino
Title	Does conversion affect short-term and oncologic outcomes after laparoscopy for colorectal cancer?
Journal	SURGICAL ENDOSCOPY
Year of publication	2013
Volume	27
pages	4596
	4607
WOS Impact factor	3.313
Type of publication	Original Article

Authors	M. Morino; M.E. Allaix; F. Famiglietti; M. Caldart; A. Arezzo
Title	Does peritoneal perforation affect short-and long term outcomes after transanal endoscopic microsurgery?
Journal	SURGICAL ENDOSCOPY
Year of publication	2013
Volume	27
pages	181
	188
WOS Impact factor	3.313

Type of publication	Original Article
Authors	Alberto Arezzo;Arianna Menciassi;Pietro Valdastri;Gastone Ciuti;Gioia Lucarini;Marco Salerno;Christian Di Natali;Mauro Verra;Paolo Dario;Mario Morino
Title	Experimental assessment of a novel robotically-driven endoscopic capsule compared to traditional colonoscopy
Journal	DIGESTIVE AND LIVER DISEASE
Year of publication	2013
Volume	45
pages	657
	662
WOS Impact factor	2.889
Type of publication	Original Article
Authors	Alberto Arezzo;Gitana Scozzari;Federico Famiglietti;Roberto Passera;Mario Morino
Title	Is single-incision laparoscopic cholecystectomy safe? Results of a systematic review and meta-analysis
Journal	SURGICAL ENDOSCOPY
Year of publication	2013
Volume	27
pages	2293
	2304
WOS Impact factor	3.313
Type of publication	Original Article
Authors	M.E. Allaix; A. Arezzo; P. Cassoni; M. Mistrangelo; G. Giraudo; M. Morino
Title	Metastatic lymph node ratio as a prognostic factor after laparoscopic total mesorectal excision for extraperitoneal rectal cancer
Journal	SURGICAL ENDOSCOPY
Year of publication	2013
Volume	27
pages	1957

	1967
WOS Impact factor	3.313
Type of publication	Original Article
Authors	A. Meining;G. Spaun;G. Fernández-Esparrach;A. Arezzo;D. Wilhelm;J. Martinek;J. Spicak;H. Feussner;K. Fuchs;T. Hucl;S. Meisner;H. Neuhaus
Title	NOTES in Europe: summary of the working group reports of the 2012 EURO-NOTES meeting
Journal	ENDOSCOPY
Year of publication	2013
Volume	45
pages	214
	217
WOS Impact factor	5.196
Type of publication	Original Article
Authors	Raffaele Manta; Giuseppe Galloro; Benedetto Mangiavillano; Rita Conigliaro; Luigi Pasquale; Alberto Arezzo; Enzo Masci; Gabrio Bassotti; Marzio Frazzoni
Title	Over-the-scope clip (OTSC) represents an effective endoscopic treatment for acute GI bleeding after failure of conventional techniques
Journal	SURGICAL ENDOSCOPY
Year of publication	2013
Volume	27
pages	3162
	3164
WOS Impact factor	3.313
Type of publication	Original Article
Authors	Mario Morino;Marco Ettore Allaix;Simone Arolfo;Alberto Arezzo
Title	Previous transanal endoscopic microsurgery for rectal cancer represents a risk factor for an increased abdominoperineal resection rate
Journal	SURGICAL ENDOSCOPY
Year of publication	2013
Volume	27

pages	3315
	3321
WOS Impact factor	3.313
Type of publication	Original Article
Authors	Alberto Arezzo;Carsten Zornig;Hamid Mofid;Karl-Hermann Fuchs;Wolfram Breithaupt;José Noguera;Georg Kaehler;Richard Magdeburg;Silvana Perretta;Bernard Dallemagne;Jacques Marescaux;Catalin Copaescu;Florin Graur;Andrei Szasz;Antonello Forgione;Raffaele Pugliese;Gerhard Buess;Hemanga K. Bhattacharjee;Giuseppe Navarra;Mario Godina;Kirill Shishin;Mario Morino
Title	The EURO-NOTES clinical registry for natural orifice transluminal endoscopic surgery: a 2-year activity report
Journal	SURGICAL ENDOSCOPY
Year of publication	2013
Volume	27
pages	3073
	3084
WOS Impact factor	3.313
Type of publication	Original Article
Authors	Alberto Arezzo;Alberto Bullano;Harald Fischer;Mario Morino
Title	The way to remove an over-the-scope-clip (with video)
Journal	GASTROINTESTINAL ENDOSCOPY
Year of publication	2013
Volume	77
pages	974
	975
WOS Impact factor	4.9
Type of publication	Original Article
Authors	Rimonda R; Arezzo A; Arolfo S; Salvai A; Morino M
Title	TransAnal Minimally Invasive Surgery (TAMIS) with SILS™ Port versus Transanal Endoscopic Microsurgery (TEM): a comparative experimental study
Journal	SURGICAL ENDOSCOPY

Year of publication	2013
Volume	27
pages	3762
	3768
WOS Impact factor	3.313
Type of publication	Original Article

Authors	M. Morino; A. Arezzo; M.E. Allaix
Title	Transanal endoscopic microsurgery
Journal	TECHNIQUES IN COLOPROCTOLOGY
Year of publication	2013
Volume	17
pages	55
	61
WOS Impact factor	1.353
Type of publication	Original Article

Authors	M.E. Allaix; A. Arezzo; S. Arolfo; M. Caldart; F. Rebecchi; M. Morino
Title	Transanal endoscopic microsurgery for rectal neoplasms. How I do it
Journal	JOURNAL OF GASTROINTESTINAL SURGERY
Year of publication	2013
Volume	17
pages	586
	592
WOS Impact factor	2.391
Type of publication	Original Article

Authors	A Arezzo;M Verra;R Reddavid;M Augusto Bonino;M Morino
Title	Treatment of Lower-GI Post-Surgical Fistulas With the Over-the-Scope Clip
Journal	VIDEO JOURNAL AND ENCYCLOPEDIA OF GI ENDOSCOPY
Year of publication	2013
Volume	1

pages	415
	418
WOS Impact factor	
Type of publication	Original Article
Authors	G. Ciuti; M. Salerno; G. Lucarini; P. Valdastri; A. Arezzo; A. Menciassi; M. Morino; P. Dario
Title	A comparative evaluation of control interfaces for a robotic-aided endoscopic capsule platform
Journal	IEEE TRANSACTIONS ON ROBOTICS
Year of publication	2012
Volume	28
pages	534
	538
WOS Impact factor	2.571
Type of publication	Original Article
Authors	G.A. Binda; A. Amato; A. Serventi; A. Arezzo
Title	Clinical presentations and risks
Journal	DIGESTIVE DISEASES
Year of publication	2012
Volume	30
pages	100
	107
WOS Impact factor	2.725
Type of publication	Original Article
Authors	Repici A; Hassan C; De Paula Pessoa D; Pagano N; Arezzo A; Zullo A; Lorenzetti R; Marmo R.
Title	Efficacy and safety of endoscopic submucosal dissection for colorectal neoplasia: a systematic review.
Journal	ENDOSCOPY
Year of publication	2012
Volume	44

pages	137
	150
WOS Impact factor	5.735
Type of publication	Original Article
Authors	A. Arezzo; M. Verra; R. Reddavid; F. Cravero; M.A. Bonino; M. Morino
Title	Efficacy of the over-the-scope clip (OTSC) for treatment of colorectal postsurgical leaks and fistulas
Journal	SURGICAL ENDOSCOPY
Year of publication	2012
Volume	26
pages	3330
	3333
WOS Impact factor	3.427
Type of publication	Original Article
Authors	P. Valdastri; G. Ciuti; A. Verbeni; A. Menciassi; P. Dario; A. Arezzo; M. Morino
Title	Magnetic air capsule robotic system: proof of concept of a novel approach for painless colonoscopy
Journal	SURGICAL ENDOSCOPY
Year of publication	2012
Volume	26
pages	1238
	1246
WOS Impact factor	3.427
Type of publication	Original Article
Authors	Gian Andrea Binda; Alberto Arezzo; Alberto Serventi; Luigina Bonelli; on behalf of the Italian Study Group on Complicated Diverticulosis (GISDIC)
Title	Multicentre observational study of the natural history of left-sided acute diverticulitis
Journal	BRITISH JOURNAL OF SURGERY
Year of publication	2012
Volume	99

pages	276
	285
WOS Impact factor	4.839
Type of publication	Original Article
Authors	S. Rocchietto; G. Scozzari; A. Arezzo; M. Morino
Title	Obese Women's Perception of bariatric trans-vaginal NOTES
Journal	OBESITY SURGERY
Year of publication	2012
Volume	22
pages	452
	459
WOS Impact factor	3.102
Type of publication	Original Article
Authors	M.E. Allaix; A. Arezzo; P. Cassoni; F. Famiglietti; M. Morino
Title	Recurrence after transanal endoscopic microsurgery for large rectal adenomas
Journal	SURGICAL ENDOSCOPY
Year of publication	2012
Volume	26
pages	2594
	2600
WOS Impact factor	3.427
Type of publication	Original Article
Authors	Allaix M.E.; Arezzo A.; Giraudo G.; Morino M.
Title	Transanal endoscopic microsurgery vs. laparoscopic total mesorectal excision for T2N0 rectal cancer
Journal	JOURNAL OF GASTROINTESTINAL SURGERY
Year of publication	2012
Volume	16
pages	2280
	2287

WOS Impact factor	2.361
Type of publication	Original Article
Authors	S. Tognarelli; V. Pensabene; S. Condino; P. Valdastri; A. Menciassi; A. Arezzo; P. Dario
Title	A pilot study on a new anchoring mechanism for surgical applications based on mucoadhesives
Journal	MINIMALLY INVASIVE THERAPY & ALLIED TECHNOLOGIES
Year of publication	2011
Volume	20
pages	3
	13
WOS Impact factor	943
Type of publication	Original Article
Authors	A. Arezzo; M. Verra; F. Cravero; Rossella Reddavid; M. Morino
Title	How to place hemoclips to achieve hemostasis of a bleeding diverticulum
Journal	DIGESTIVE DISEASES AND SCIENCES
Year of publication	2011
Volume	56
pages	1589
	1591
WOS Impact factor	2.117
Type of publication	Original Article
Authors	A. Arezzo; M. Verra; A. Miegge; M. Morino
Title	Loop-and-go technique for a bleeding, large sessile gastric gastrointestinal stromal tumor (GIST)
Journal	ENDOSCOPY
Year of publication	2011
Volume	43
pages	E18
	E19

WOS Impact factor	5.21
Type of publication	Original Article
Authors	Pensabene V; Valdastri P; Tognarelli S; Menciassi A; Arezzo A; Dario P
Title	Mucoadhesive film for anchoring assistive surgical instruments in endoscopic surgery: in vivo assessment of deployment and attachment.
Journal	SURGICAL ENDOSCOPY
Year of publication	2011
Volume	25
pages	3071
	3079
WOS Impact factor	4.013
Type of publication	Original Article
Authors	M. Morino; M. Verra; F. Famiglietti; A. Arezzo
Title	Natural Orifice Transluminal Endoscopic Surgery (NOTES) and colorectal cancer?
Journal	COLORECTAL DISEASE
Year of publication	2011
Volume	13
pages	47
	50
WOS Impact factor	2.927
Type of publication	Original Article
Authors	M. Morino; M. Ettore Allaix; M. Caldart; G. Scozzari; A. Arezzo
Title	Risk factors for recurrence after transanal endoscopic microsurgery for rectal malignant neoplasm
Journal	SURGICAL ENDOSCOPY
Year of publication	2011
Volume	25
pages	3683
	3690

WOS Impact factor	4.013
Type of publication	Original Article
Authors	Arezzo A; Podzemny V; Pescatori M.
Title	Surgical management of hemorrhoids. State of the art
Journal	ANNALI ITALIANI DI CHIRURGIA
Year of publication	2011
Volume	82
pages	163
	172
WOS Impact factor	231
Type of publication	Original Article
Authors	Arezzo A; Verra M; Morino M
Title	Transanal endoscopic microsurgery after neoadjuvant therapy for rectal GIST
Journal	DIGESTIVE AND LIVER DISEASE
Year of publication	2011
Volume	43
pages	923
	924
WOS Impact factor	3.054
Type of publication	Original Article
Authors	P. Valdastri; C. Quaglia; E. Buselli; A. Arezzo; N. Di Lorenzo; M. Morino; A. Menciassi; P. Dario
Title	A magnetic internal mechanism for camera steering in wireless endoluminal applications
Journal	ENDOSCOPY
Year of publication	2010
Volume	42
pages	481
	486
WOS Impact factor	6.096

Type of publication	Original Article
Authors	A. Arezzo; A. Miegge; A. Garbarini; M. Morino
Title	Endoluminal vacuum therapy for anastomotic leaks after rectal surgery
Journal	TECHNIQUES IN COLOPROCTOLOGY
Year of publication	2010
Volume	14
pages	279
	281
WOS Impact factor	1.533
Type of publication	Original Article
Authors	A. Arezzo; M. Morino
Title	Endoscopic closure of gastric access in perspective NOTES : an update on techniques and technologies
Journal	SURGICAL ENDOSCOPY
Year of publication	2010
Volume	24
pages	298
	303
WOS Impact factor	3.436
Type of publication	Original Article
Authors	G. Scozzari; A. Arezzo; M. Morino
Title	Enterovesical fistulas: diagnosis and management
Journal	TECHNIQUES IN COLOPROCTOLOGY
Year of publication	2010
Volume	14
pages	293
	300
WOS Impact factor	1.533
Type of publication	Original Article

Authors	Nereo Vettoretto; Alberto Arezzo
Title	Human natural orifice translumenal endoscopic surgery: on the way to two different philosophies?
Journal	SURGICAL ENDOSCOPY
Year of publication	2010
Volume	24
pages	490
	492
WOS Impact factor	3.436
Type of publication	Original Article
Authors	G. Ciusti; R. Dolin; P. Valdastri; A. Arezzo; A. Menciassi; M. Morino; P. Dario
Title	Robotic versus manual control in magnetic steering of an endoscopic capsule
Journal	ENDOSCOPY
Year of publication	2010
Volume	42
pages	148
	152
WOS Impact factor	6.096
Type of publication	Original Article
Authors	A. Arezzo; A. Miegge; A. Garbarini; M. Morino
Title	Trattamento delle deiscenze chirurgiche del retto mediante Endo-Vac therapy
Journal	GIORNALE ITALIANO DI ENDOSCOPIA DIGESTIVA
Year of publication	2010
Volume	33
pages	71
	73
WOS Impact factor	
Type of publication	Original Article
Authors	M. Morino; A. Arezzo

Title	Video Surgery through single port access: an overview
Journal	REVISTA PORTUGUESA DE CIRURGIA
Year of publication	2010
Volume	13
pages	9
	11
WOS Impact factor	
Type of publication	Original Article
Authors	A. Repici; A. Arezzo; G. De Caro; M. Morino; N. Pagano; G. Rando; F. Romeo; G. Del Conte; S. Danese; A. Malesci
Title	Clinical Experience with a new endoscopic over-the scope clip system for use in the GI tract
Journal	DIGESTIVE AND LIVER DISEASE
Year of publication	2009
Volume	41
pages	406
	410
WOS Impact factor	2.972
Type of publication	Original Article
Authors	R. Rimonda; A. Arezzo; C. Garrone; ME Allaix; G. Giraudo; M. Morino
Title	Electrothermal bipolar vessel sealing system vs. harmonic scalpel in colorectal laparoscopic surgery: A prospective, randomized study
Journal	DISEASES OF THE COLON & RECTUM
Year of publication	2009
Volume	52
pages	657
	661
WOS Impact factor	2.536
Type of publication	Original Article
Authors	A. Arezzo; N. Pagano; F. Romeo; G. Delconte; C. Hervoso; M. Morino; A. Repici

Title	Hydroxy-propyl-methyl-cellulose is a safe and effective lifting agent for endoscopic mucosal resection of large colorectal polyps
Journal	SURGICAL ENDOSCOPY
Year of publication	2009
Volume	23
pages	1065
	1069
WOS Impact factor	3.307
Type of publication	Original Article
Authors	Saccomani G; Arezzo A; Percivale A; Baldo S; Pellicci R.
Title	Laparoscopic cholecystectomy can be performed safely with only three ports in the majority of cases.
Journal	CHIRURGIA ITALIANA
Year of publication	2009
Volume	61
pages	613
	616
WOS Impact factor	
Type of publication	Original Article
Authors	A. Arezzo; T. Kratt; M.O. Schurr; M. Morino
Title	Laparoscopic-assisted transgastric cholecystectomy and secure endoscopic closure of the transgastric defect in a survival porcine model
Journal	ENDOSCOPY
Year of publication	2009
Volume	41
pages	767
	772
WOS Impact factor	5.545
Type of publication	Original Article
Authors	Arezzo A; Garbarini A; Foco A; Morino M.

Title	Rimozione per via endoscopica di Swedish Adjustable Gastric Band migrato in sede intragastrica.
Journal	GIORNALE ITALIANO DI ENDOSCOPIA DIGESTIVA
Year of publication	2009
Volume	32
pages	145
	147
WOS Impact factor	
Type of publication	Original Article
Authors	Arezzo A; Pescatori M.
Title	Surgical procedures for evacuatory disorders
Journal	ANNALI ITALIANI DI CHIRURGIA
Year of publication	2009
Volume	80
pages	261
	266
WOS Impact factor	281
Type of publication	Original Article
Authors	Allaix M.E.; Arezzo A; Caldart M.; Festa F.; Morino M.
Title	Transanal endoscopic microsurgery for rectal neoplasms: experience of 300 consecutive cases
Journal	DISEASES OF THE COLON & RECTUM
Year of publication	2009
Volume	52
pages	1831
	1836
WOS Impact factor	2.536
Type of publication	Original Article
Authors	A. Arezzo; G. Giraudo; M.E. Allaix; E.M. Targarona; M. Morino
Title	"ESCO Trial" - Le stent intestinal dans l'occlusion coliquë aigue par cancer

Journal	LE JOURNAL DE COELIO-CHIRURGIE
Year of publication	2008
Volume	68
pages	36
	41
WOS Impact factor	
Type of publication	Original Article
Authors	SCHURR MO; KALANOVIC D; AREZZO A; FLEISCH C; BUESS G
Title	Development of a transoral fundoplication device and related experimental research
Journal	MINIMALLY INVASIVE THERAPY & ALLIED TECHNOLOGIES
Year of publication	2008
Volume	17
pages	50
	56
WOS Impact factor	1.611
Type of publication	Original Article
Authors	A. Repici; N. Pagano; A. Arezzo
Title	Endoscopic submucosal dissection technique (Tecnica della endoscopic submucosal dissection)
Journal	GIORNALE ITALIANO DI ENDOSCOPIA DIGESTIVA
Year of publication	2008
Volume	31
pages	59
	64
WOS Impact factor	
Type of publication	Original Article
Authors	Repici A; Pagano N; Arezzo A
Title	Tecnica della Endoscopic Submucosal Dissection.
Journal	GIORNALE ITALIANO DI ENDOSCOPIA DIGESTIVA

Year of publication	2008
Volume	31
pages	59
	64
WOS Impact factor	
Type of publication	Original Article

Authors	Schurr MO; Arezzo A; Ho CN; Anhoeck G; Buess G; Di Lorenzo N.
Title	The OTSC clip for endoscopic organ closure in NOTES: device and technique.
Journal	MINIMALLY INVASIVE THERAPY & ALLIED TECHNOLOGIES
Year of publication	2008
Volume	17
pages	262
	266
WOS Impact factor	1.611
Type of publication	Original Article

Authors	M. Morino; A. Arezzo
Title	Video-laparo-colecistectomia con tecnica standardizzata alla francese
Journal	OSPEDALI D'ITALIA. CHIRURGIA
Year of publication	2008
Volume	14
pages	311
	320
WOS Impact factor	
Type of publication	Original Article

Authors	REPICI A; CONIO M; DE ANGELIS C; SAPINO A; MALESCI A; AREZZO A; HERVOSO C; PELLICANO R; COMUNALE S; RIZZETTO M
Title	Insulated-tip knife endoscopic mucosal resection of large colorectal polyps unsuitable for standard polypectomy
Journal	AMERICAN JOURNAL OF GASTROENTEROLOGY
Year of publication	2007

Volume	102(8)
pages	1617
	1623
WOS Impact factor	6.101
Type of publication	Original Article
Authors	LIRICI MM; AREZZO A
Title	Surgery without scars: the new frontier of minimally invasive surgery? Controversies, concerns and expectations in advanced operative endoscopy
Journal	MINIMALLY INVASIVE THERAPY & ALLIED TECHNOLOGIES
Year of publication	2006
Volume	15
pages	323
	324
WOS Impact factor	425
Type of publication	Original Article
Authors	SACCOMANI G; DURANTE V; MAGNOLIA MR; GHEZZO L; LOMBEZZI R; ESERCIZIO L; STELLA M; AREZZO A
Title	Combined endoscopic treatment for cholelithiasis associated with choledocholithiasis
Journal	SURGICAL ENDOSCOPY
Year of publication	2005
Volume	19
pages	910
	914
WOS Impact factor	1.746
Type of publication	Original Article
Authors	AREZZO A; SCHURR MO; BRAUN A; BUESS GF
Title	Experimental assessment of a new mechanical endoscopic solosurgery system: Endofreeze
Journal	SURGICAL ENDOSCOPY
Year of publication	2005

Volume	19(4)
pages	581
	588
WOS Impact factor	1.746
Type of publication	Original Article
Authors	AGRESTA F; DE SIMONE P; LEONE L; AREZZO A; BIONDI A; BOTTERO L; CATENA F; CONZO G; DEL GENIO G; FERSINI A; GUERRIERI M; ILLOMEI G; TONELLI P; VITELLARO M; DOCIMO G; CRUCITTI A
Title	Laparoscopic appendectomy in Italy: an appraisal of 26,863 cases
Journal	JOURNAL OF LAPAROENDOSCOPIC & ADVANCED SURGICAL TECHNIQUES.
Year of publication	2004
Volume	14
pages	1
	8
WOS Impact factor	862
Type of publication	Original Article
Authors	A. AREZZO; TESTA T; SCHURR MO; BUESS GF; DE GREGORI M
Title	Robotic and systems technology for advanced endoscopic procedures
Journal	ANNALI ITALIANI DI CHIRURGIA
Year of publication	2001
Volume	72
pages	467
	472
WOS Impact factor	
Type of publication	Original Article
Authors	BUESS GF; A. AREZZO; SCHURR MO; ULMER F; FISHER H; GUMB L; TESTA T; NOBMAN C
Title	A new remote-controlled endoscope positioning system for endoscopic solo surgery. The FIPS endoarm.
Journal	SURGICAL ENDOSCOPY

Year of publication	2000
Volume	14
pages	395
	399
WOS Impact factor	2.056
Type of publication	Original Article
Authors	S.C. FISCHER; K. ROTH; A. AREZZO; H. RAESTRUP; M.O. SCHURR; G.F. BUESS
Title	Comparative Study of the Use of a Suturing System and Titanium Clips.
Journal	SURGICAL TECHNOLOGY INTERNATIONAL
Year of publication	2000
Volume	9
pages	141
	145
WOS Impact factor	
Type of publication	Original Article
Authors	A. AREZZO; F. ULMER; O. WEISS; M.O. SCHURR; M. HAMAD; G.F. BUESS
Title	Experimental trial on solo surgery for minimally invasive therapy: comparison of different systems in a phantom model.
Journal	SURGICAL ENDOSCOPY
Year of publication	2000
Volume	14
pages	955
	959
WOS Impact factor	2.056
Type of publication	Original Article
Authors	A. AREZZO; TESTA T; ULMER F; SCHURR MO; DEGREGORI M; BUESS GF
Title	Positioning systems for endoscopic solo surgery
Journal	MINERVA CHIRURGICA
Year of publication	2000

Volume	55
pages	635
	641.
WOS Impact factor	
Type of publication	Original Article
Authors	A. AREZZO
Title	Prospective randomized trial comparing bowel cleaning preparations for colonoscopy.
Journal	SURGICAL LAPAROSCOPY ENDOSCOPY & PERCUTANEOUS TECHNIQUES
Year of publication	2000
Volume	10(4)
pages	215
	217
WOS Impact factor	691
Type of publication	Original Article
Authors	A. AREZZO; KEES T; KUNERT W; DE GREGORI M; BUESS G
Title	Shadow optic. An endoscope with optimized ligth
Journal	CHIRURGIA ITALIANA
Year of publication	2000
Volume	52
pages	451
	453
WOS Impact factor	
Type of publication	Original Article
Authors	SCHURR MO; A. AREZZO; BUESS GF
Title	Robotics and systems technology for advanced endoscopic procedures: experiences in general surgery
Journal	EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY
Year of publication	1999
Volume	16

pages	97
	105
WOS Impact factor	1.134
Type of publication	Original Article
Authors	SCHURR MO; KUNERT W; AREZZO A; BUESS G
Title	The role and future of endoscopic imaging systems.
Journal	ENDOSCOPY
Year of publication	1999
Volume	31
pages	557
	562
WOS Impact factor	1.726
Type of publication	Original Article
Authors	SCHURR MO ;AREZZO A ;NEISIUS B ;RININSLAND H ;HILZINGER HU ;DORN J ;ROTH K ;BUESS GF
Title	Trocar and instrument positioning system TISKA. An assist device for endoscopic solo surgery.
Journal	SURGICAL ENDOSCOPY
Year of publication	1999
Volume	13
pages	528
	531
WOS Impact factor	2.24
Type of publication	Original Article
Authors	De Salvo L; Arezzo A; Razzetta F; Tassone U; Mattioli FP
Title	Connection between the type of drainage and sepsis in thyroid surgery
Journal	ANNALI ITALIANI DI CHIRURGIA
Year of publication	1998
Volume	69
pages	165

	167
WOS Impact factor	
Type of publication	Original Article
Authors	AREZZO A ;GUALCO M ;BIANCHI C ;BORGONOVO G ;LAPERTOSA G ;TORRE G
Title	Immature malignant teratoma of the thyroid gland.
Journal	JOURNAL OF EXPERIMENTAL & CLINICAL CANCER RESEARCH
Year of publication	1998
Volume	17(1)
pages	109
	112
WOS Impact factor	257
Type of publication	Original Article
Authors	G. TORRE; G. BORGONOVO; A. AREZZO; M. COSTANTINI; E. VARALDO; G.L. ANSALDO; F.P. MATTIOLI
Title	Is euthyroidism the goal of surgical treatment of diffuse toxic goitre?
Journal	EUROPEAN JOURNAL OF SURGERY
Year of publication	1998
Volume	164
pages	495
	500
WOS Impact factor	795
Type of publication	Original Article
Authors	A. AREZZO; PATETTA R; CEPPA P; BORGONOVO G; TORRE G; MATTIOLI FP
Title	Mucoepidermoid carcinoma of the thyroid gland arising from a papillary epithelial neoplasm.
Journal	THE AMERICAN SURGEON
Year of publication	1998
Volume	64
pages	307

	311
WOS Impact factor	994
Type of publication	Original Article
Authors	L. DE SALVO; F. RAZZETTA; U. TASSONE; A. AREZZO; FP. MATTIOLI
Title	The role of drainage and antibiotic prophylaxis in thyroid surgery.
Journal	MINERVA CHIRURGICA
Year of publication	1998
Volume	53
pages	895
	898
WOS Impact factor	
Type of publication	Original Article
Authors	PINDUCCIU C; BORGONOVO G; A. AREZZO; TORRE GC; GIORDANO G; CORDERA R
Title	Toxic thyroid adenoma: absence of DNA mutations of the TSH receptor and Gs alpha.
Journal	EUROPEAN JOURNAL OF ENDOCRINOLOGY
Year of publication	1998
Volume	138
pages	37
	40
WOS Impact factor	2.101
Type of publication	Original Article
Authors	L. DE SALVO; F. RAZZETTA; A. CAGNAZZO; U. TASSONE; A. AREZZO; F.P. MATTIOLI
Title	Comparison of colorectal mechanical suture techniques
Journal	ANNALI ITALIANI DI CHIRURGIA
Year of publication	1997
Volume	68
pages	381

	384
WOS Impact factor	
Type of publication	Original Article
Authors	G. BORGONOVO; F. RAZZETTA; A. AREZZO; G. TORRE; F. MATTIOLI
Title	Giant hemangiomas of the liver: surgical treatment by liver resection.
Journal	HEPATO-GASTROENTEROLOGY
Year of publication	1997
Volume	44
pages	231
	234
WOS Impact factor	
Type of publication	Original Article
Authors	DE SALVO L; RAZZETTA F; AREZZO A; TASSONE U; BOGLIOLO G; BRUZZONE D; MATTIOLI F
Title	Surveillance after colorectal cancer surgery
Journal	EUROPEAN JOURNAL OF SURGICAL ONCOLOGY
Year of publication	1997
Volume	23
pages	522
	525
WOS Impact factor	
Type of publication	Original Article
Authors	TORRE G; BORGONOVO G; AMATO A; AREZZO A; DE NEGRI A; MATTIOLI FP
Title	Differentiated thyroid cancer: surgical treatments of 190 patients.
Journal	EUROPEAN JOURNAL OF SURGICAL ONCOLOGY
Year of publication	1996
Volume	22(3)
pages	276
	281

WOS Impact factor	
Type of publication	Original Article

Reviews

Authors	Arezzo, Alberto; Passera, Roberto; Lo Secco, Giacomo; Verra, Mauro; Bonino, Marco Augusto; Targarona, Eduardo; Morino, Mario
Title	Stent as bridge to surgery for left-sided malignant colonic obstruction reduces adverse events and stoma rate compared with emergency surgery: results of a systematic review and meta-analysis of randomized controlled trials
Journal	GASTROINTESTINAL ENDOSCOPY
Year of publication	2017
Volume	86(3)
pages	416
	426
WOS Impact factor	6.501
Type of publication	Original Article

Authors	Tabola, R; Cirocchi, R; Fingerhut, A; Arezzo, A; Randolph, J; Grassi, V; Binda, G A; D'Andrea, V; Abraha, I; Popivanov, G; Di Saverio, S; Zbar, A
Title	A systematic analysis of controlled clinical trials using the NiTi CAR™ compression ring in colorectal anastomoses
Journal	TECHNIQUES IN COLOPROCTOLOGY
Year of publication	2017
Volume	21
pages	177
	184
WOS Impact factor	2.342
Type of publication	Review

Authors	Cirocchi, R.; Di Saverio, S; Weber, D.G.; Taboła, R.; Abraha, I.; Randolph, J.; Arezzo, A.; Binda, G.A.
Title	Laparoscopic lavage versus surgical resection for acute diverticulitis with generalised peritonitis: a systematic review and meta-analysis
Journal	TECHNIQUES IN COLOPROCTOLOGY

Year of publication	2017
Volume	21
pages	1
	18
WOS Impact factor	2.342
Type of publication	Review

Authors	Arezzo, Alberto; Bini, Roberto; Secco, Giacomo Lo; Verra, Mauro; Passera, Roberto
Title	The role of stents in the management of colorectal complications: a systematic review
Journal	SURGICAL ENDOSCOPY
Year of publication	2017
Volume	31
pages	2720
	2730
WOS Impact factor	3.747
Type of publication	Review

Authors	Birindelli, Arianna; Di Saverio, Salomone; Agresta, Ferdinando; Mandrioli, Matteo; Tugnoli, Gregorio; Arezzo, Alberto
Title	A Comparison of Laparoscopy and Laparotomy for the Management of Abdominal Trauma: A Systematic Review and Meta-analysis
Journal	WORLD JOURNAL OF SURGERY
Year of publication	2016
Volume	40
pages	1524
	1525
WOS Impact factor	2.673
Type of publication	Review

Authors	Agresta, Ferdinando; Arezzo, Alberto; Allaix, Marco Ettore; Arolfo, Simone; Anania, Gabriele
Title	Current status of laparoscopic colorectal surgery in the emergency setting
Journal	UPDATES IN SURGERY
Year of publication	2016
Volume	68
pages	47
	52
WOS Impact factor	
Type of publication	Review
Authors	Allaix, Marco Ettore; Furnée, Edgar J B; Arezzo, Alberto; Mistrangelo, Massimiliano; Morino, Mario
Title	Energy Sources for Laparoscopic Colorectal Surgery: Is One Better than the Others?
Journal	JOURNAL OF LAPAROENDOSCOPIC & ADVANCED SURGICAL TECHNIQUES.
Year of publication	2016
Volume	26
pages	264
	269
WOS Impact factor	1.255
Type of publication	Review
Authors	Ciuti, Gastone; Caliò, R.; Camboni, D.; Neri, L.; Bianchi, F.; Arezzo, A.;

	Koulaouzidis, A.; Schostek, S.; Stoyanov, D.; Oddo, C. M.; Magnani, B.; Menciassi, A.; Morino, M.; Schurr, M. O.; Dario, P.
Title	Frontiers of robotic endoscopic capsules: a review
Journal	JOURNAL OF MICRO-BIO ROBOTICS
Year of publication	2016
Volume	11
pages	1
	18
WOS Impact factor	
Type of publication	Review
Authors	Cirocchi, Roberto; D'Andrea, Vito; Arezzo, Alberto; Abraha, Iosief; Passera, Roberto; Avenia, Nicola; Randolph, Justus; Barczyñski, Marcin
Title	Intraoperative neuromonitoring versus visual nerve identification for prevention of recurrent laryngeal nerve injury in adults undergoing thyroid surgery
Journal	COCHRANE DATABASE OF SYSTEMATIC REVIEWS
Year of publication	2016
Volume	2016
pages	1
	18
WOS Impact factor	6.124
Type of publication	Review
Authors	Mangiavillano, Benedetto; Caruso, Angelo; Manta, Raffaele; Di Mitri, Roberto; Arezzo, Alberto; Pagano, Nico; Galloro, Giuseppe; Mocciaro, Filippo; Mutignani, Massimiliano; Luigiano, Carmelo; Antonucci, Enrico; Conigliaro, Rita; Masci, Enzo
Title	Over-the-scope clips in the treatment of gastrointestinal tract iatrogenic perforation: A multicenter retrospective study and a classification of gastrointestinal tract perforations
Journal	WORLD JOURNAL OF GASTROINTESTINAL SURGERY
Year of publication	2016
Volume	8
pages	315
	320

WOS Impact factor	
Type of publication	Review
Authors	Arezzo, A.; Passera, R.; Marchese, N.; Galloro, G.; Manta, R.; Cirocchi, R.
Title	Systematic review and meta-analysis of endoscopic submucosal dissection vs endoscopic mucosal resection for colorectal lesions
Journal	UNITED EUROPEAN GASTROENTEROLOGY JOURNAL
Year of publication	2016
Volume	4
pages	18
	29
WOS Impact factor	3.673
Type of publication	Review
Authors	Allaix, Marco E; Arezzo, Alberto; Morino, Mario
Title	Transanal endoscopic microsurgery for rectal cancer: T1 and beyond? An evidence-based review
Journal	SURGICAL ENDOSCOPY
Year of publication	2016
Volume	30
pages	4841
	4852
WOS Impact factor	3.747
Type of publication	Review
Authors	Manta, R; Tremolaterra, F; Arezzo, A; Verra, M; Galloro, G; Dioscoridi, L; Pugliese, F; Zullo, A; Mutignani, M; Bassotti, G
Title	Complications during colonoscopy: prevention, diagnosis, and management
Journal	TECHNIQUES IN COLOPROCTOLOGY

Year of publication	2015
Volume	19
pages	505
	513
WOS Impact factor	2.32
Type of publication	Review
Authors	A. Arezzo;R. Passera;M. Migliore;R. Cirocchi;G. Galloro;R. Manta;M. Morino
Title	Efficacy and safety of laparo-endoscopic resections of colorectal neoplasia: A systematic review
Journal	UNITED EUROPEAN GASTROENTEROLOGY JOURNAL
Year of publication	2015
Volume	3
pages	514
	522
WOS Impact factor	2.933
Type of publication	Review
Authors	Cirocchi, Roberto; Arezzo, Alberto; Renzi, Claudio; Cochetti, Giovanni; D'Andrea, Vito; Fingerhut, Abe; Mearini, Ettore; Binda, Gian Andrea
Title	Is laparoscopic surgery the best treatment in fistulas complicating diverticular disease of the sigmoid colon? A systematic review
Journal	INTERNATIONAL JOURNAL OF SURGERY
Year of publication	2015
Volume	24
pages	95
	100
WOS Impact factor	1.657
Type of publication	Review
Authors	R. Cirocchi; S. Trastulli; N. Vettoretto; D. Milani; D. Cavaliere; C. Renzi; O. Adamenko; J. Desiderio; M.F. Burattini; A. Parisi; A. arezzo; A. Fingerhut

Title	Laparoscopic peritoneal lavage: A definitive treatment for diverticular peritonitis or a "bridge" to elective laparoscopic sigmoidectomy?
Journal	MEDICINE
Year of publication	2015
Volume	94
pages	1
	14
WOS Impact factor	2.133
Type of publication	Review
Authors	Arezzo, Alberto; Passera, Roberto; Ferri, Valentina; Gonella, Federica; Cirocchi, Roberto; Morino, Mario
Title	Laparoscopic right colectomy reduces short-term mortality and morbidity. Results of a systematic review and meta-analysis
Journal	INTERNATIONAL JOURNAL OF COLORECTAL DISEASE
Year of publication	2015
Volume	30
pages	1457
	1472
WOS Impact factor	2.383
Type of publication	Review
Authors	Alberto Arezzo;Roberto Passera;Alessandro Salvai;Simone Arolfo;Marco Ettore Allaix;Guido Schwarzer;Mario Morino
Title	Laparoscopy for rectal cancer is oncologically adequate: a systematic review and meta-analysis of the literature
Journal	SURGICAL ENDOSCOPY
Year of publication	2015
Volume	29
pages	334
	348
WOS Impact factor	3.54

Type of publication	Review
Authors	Arezzo A; Verra M; Passera R; Bullano A; Rapetti L; Morino M
Title	Long-term efficacy of endoscopic vacuum therapy for the treatment of colorectal anastomotic leaks
Journal	DIGESTIVE AND LIVER DISEASE
Year of publication	2015
Volume	47
pages	342
	345
WOS Impact factor	2.719
Type of publication	Review
Authors	Cirocchi, Roberto; Grassi, Veronica; Cavaliere, Davide; Renzi, Claudio; Tabola, Renata; Poli, Giulia; Avenia, Stefano; Farinella, Eleonora; Arezzo, Alberto; Vettoretto, Nereo; D'Andrea, Vito; Binda, Gian Andrea; Fingerhut, Abe
Title	New Trends in Acute Management of Colonic Diverticular Bleeding
Journal	MEDICINE
Year of publication	2015
Volume	94
pages	1710
	1716
WOS Impact factor	2.133
Type of publication	Review
Authors	A. Arezzo;T. Matsuda;B. Rembacken;W. F. A. Miles;G. Coccia;Y. Saito
Title	Piecemeal mucosectomy, submucosal dissection or transanal microsurgery for large colorectal neoplasm
Journal	COLORECTAL DISEASE
Year of publication	2015
Volume	17
pages	44
	51

WOS Impact factor	2.452
Type of publication	Review
Authors	Cirocchi, Roberto; Trastulli, Stefano; Randolph, Justus; Guarino, Salvatore; Di Rocco, Giorgio; Arezzo, Alberto; D'Andrea, Vito; Santoro, Alberto; Barczyñski, Marcin; Avenia, Nicola
Title	Total or near-total thyroidectomy versus subtotal thyroidectomy for multinodular non-toxic goitre in adults
Journal	COCHRANE DATABASE OF SYSTEMATIC REVIEWS
Year of publication	2015
Volume	Art. No: CD010370
pages	1
	55
WOS Impact factor	6.103
Type of publication	Review
Authors	Arezzo, Alberto; Cochetti, Giovanni G; Cirocchi, Roberto; Randolph, Justus J; Mearini, Ettore E; Passera, Roberto
Title	Transperitoneal versus retroperitoneal laparoscopic adrenalectomy for adrenal tumours in adults
Journal	COCHRANE DATABASE OF SYSTEMATIC REVIEWS
Year of publication	2015
Volume	
pages	1
	10
WOS Impact factor	6.103
Type of publication	Review
Authors	Roberto Cirocchi ; Umberto Morelli ; Alberto Arezzo ; Stefano Trastulli ; Amilcare Parisi ; Massimo Falconi ; Mario Morino; Jayesh Sagar
Title	Double-stapled anastomosis versus mucosectomy and handsewn anastomosis in ileal pouch-anal anastomosis for ulcerative colitis or familial adenomatous

	polyposis
Journal	COCHRANE DATABASE OF SYSTEMATIC REVIEWS
Year of publication	2014
Volume	Art. No: CD011089
pages	1
	8
WOS Impact factor	6.035
Type of publication	Review
Authors	Roberto Cirocchi;Alberto Arezzo;Nereo Vettoretto;Davide Cavaliere;Eriberto Farinella;Claudio Renzi;Gaspare Cannata;Jacopo Desiderio;Federico Farinacci;Francesco Barberini;Stefano Trastulli;Amilcare Parisi;Abe Fingerhut
Title	Role of Damage Control Surgery in the Treatment of Hinchey III and IV Sigmoid Diverticulitis
Journal	MEDICINE
Year of publication	2014
Volume	93
pages	e184
	e190
WOS Impact factor	5.723
Type of publication	Review
Authors	Cirocchi R.; Randolph JJ.; Montedori A. Cochetti GG.; Arezzo A.; Mearini EE.; Abraha I; Trastulli S.
Title	Staples versus sutures for surgical wound closure in adults (Protocol)
Journal	COCHRANE DATABASE OF SYSTEMATIC REVIEWS
Year of publication	2014
Volume	ARTICOLO N° CD011250
pages	1
	13
WOS Impact factor	6.035
Type of publication	Review

Authors (*)	Alberto Arezzo;Roberto Passera;Yutaka Saito;Taku Sakamoto;Nozomu Kobayashi;Naoto Sakamoto;Naohisa Yoshida;Yuji Naito;Mitsuhiro Fujishiro;Keiko Niimi;Tomohiko Ohya;Ken Ohata;Shinichi Okamura;Shinei Iizuka;Yoji Takeuchi;Noriya Uedo;Pietro Fusaroli;Marco Augusto Bonino;Mauro Verra;Mario Morino
Title	Systematic review and meta-analysis of endoscopic submucosal dissection versus transanal endoscopic microsurgery for large noninvasive rectal lesions
Journal	SURGICAL ENDOSCOPY
Year of publication	2014
Volume	28
pages	427
	438
WOS Impact factor	3.256
Type of publication	Review

Authors	Alberto Arezzo
Title	The past, the present, and the future of minimally invasive therapy in laparoscopic surgery: A review and speculative outlook
Journal	MINIMALLY INVASIVE THERAPY & ALLIED TECHNOLOGIES
Year of publication	2014
Volume	23
pages	253
	260
WOS Impact factor	1.271
Type of publication	Review

Authors	Alberto Arezzo;Simone Arolfo;Francesca Cravero;Marco Migliore;Marco Ettore Allaix;Mario Morino
Title	Which treatment for large rectal adenoma? Preoperative assessment and therapeutic strategy
Journal	MINIMALLY INVASIVE THERAPY & ALLIED TECHNOLOGIES

Year of publication	2014
Volume	23
pages	21
	27
WOS Impact factor	1.271
Type of publication	Review
Authors	M. Mistrangelo;M. E. Allaix;A. Arezzo;M. Morino
Title	Comments on Levic et al.: The outcome of rectal cancer after early salvage TME following TEM compared with primary TME: a case-matched study
Journal	TECHNIQUES IN COLOPROCTOLOGY
Year of publication	2013
Volume	
pages	81
	81
WOS Impact factor	1.353
Type of publication	Review
Authors	A. Arezzo; N. Vettoretto; F. Famiglietti; L. Moja; M. Morino
Title	Laparoendoscopic rendezvous reduces perioperative morbidity and risk of pancreatitis
Journal	SURGICAL ENDOSCOPY
Year of publication	2013
Volume	27
pages	1055
	1060
WOS Impact factor	3.313

Type of publication	Review
Authors	N. Vettoretto; A. Arezzo; F. Famiglietti; R. Cirocchi; L. Moja; M. Morino
Title	Laparoscopic-endoscopic rendezvous versus preoperative endoscopic sphincterotomy for common bile duct stones in patients undergoing laparoscopic cholecystectomy (Protocol)
Journal	COCHRANE DATABASE OF SYSTEMATIC REVIEWS
Year of publication	2013
Volume	-
pages	1
	11
WOS Impact factor	5.939
Type of publication	Review
Authors	A. Arezzo; R. Passera; G. Scozzari; M. Verra; M. Morino
Title	Laparoscopy for extraperitoneal rectal cancer reduces short-term morbidity: Results of a systematic review and meta-analysis
Journal	UNITED EUROPEAN GASTROENTEROLOGY JOURNAL
Year of publication	2013
Volume	1
pages	32
	47
WOS Impact factor	
Type of publication	Review
Authors	A. Arezzo; R. Passera; G. Scozzari; M. Verra; M. Morino
Title	Laparoscopy for rectal cancer reduces short-term mortality and morbidity: results of a systematic review and meta-analysis
Journal	SURGICAL ENDOSCOPY
Year of publication	2013
Volume	27
pages	1485

	1502
WOS Impact factor	3.313
Type of publication	Review
Authors	A. Arezzo; A. Repici; A. Kirschniak; M. O. Schurr; C-N Ho; M. Morino
Title	New developments for endoscopic hollow organ closure in prospective of NOTES (Review)
Journal	MINIMALLY INVASIVE THERAPY & ALLIED TECHNOLOGIES
Year of publication	2008
Volume	17
pages	355
	360
WOS Impact factor	1.611

Editorials

Authors	Arezzo, Alberto
Title	Obstrucción colónica maligna: ¿to stent or not to stent?
Journal	CIRURGIA ESPAÑOLA
Year of publication	2017
Volume	95
pages	121
	122
WOS Impact factor	1.276
Type of publication	Editorial
Authors	Arezzo, A
Title	To clip or not to clip? Invited comment on Wilhelm et al.: Use of self-retaining barbed suture for rectal wall closure in transanal endoscopic microsurgery
Journal	TECHNIQUES IN COLOPROCTOLOGY
Year of publication	2014
Volume	18
pages	841

	842
WOS Impact factor	2.342
Type of publication	Invited Comment
Authors	A. Arezzo; M. Morino
Title	Endoscopic surgery through single-port incision: time for a trial?
Journal	SURGICAL ENDOSCOPY
Year of publication	2011
Volume	25
pages	1709
	1711
WOS Impact factor	3.237
Type of publication	Editorial

Letter to the Editor

Authors	Massimiliano Mistrangelo;Alberto Arezzo;Mario Morino
Title	Comments on Decision Analysis for Patients With T1 Adenocarcinoma of the Low Rectum
Journal	DISEASES OF THE COLON & RECTUM
Year of publication	2013
Volume	56
pages	e396
	E397
WOS Impact factor	
Type of publication	Letter
Authors	Massimiliano Mistrangelo;Ilaria Giono;Alberto Arezzo
Title	Comments on Midterm Results After Perineal Stapled Prolapse Resection for External Rectal Prolapse
Journal	DISEASES OF THE COLON & RECTUM
Year of publication	2013
Volume	56

pages	e365
WOS Impact factor	
Type of publication	Letter
Authors	Alberto Arezzo; Alberto Bullano; Harald Fischer; Mario Morino
Title	The way to remove an over-the-scope-clip
Journal	GASTROINTESTINAL ENDOSCOPY
Year of publication	2013
Volume	77
pages	974 975
WOS Impact factor	
Type of publication	Letter
Authors	A. Arezzo; F. Famiglietti; M. Morino; R. Passera
Title	Should laparoscopic colorectal surgery still be considered unsafe?
Journal	ANNALS OF SURGERY
Year of publication	2012
Volume	256
pages	e22
WOS Impact factor	
Type of publication	Letter

BOOKS/CHAPTERS/THESIS

Chapters

Authors	Simone, Arolfo; Arezzo, Alberto
Title	TEM and TAMIS for large rectal neoplasm
Year of publication	2017
pages	67
	81
Book title	Diagnosis and Endoscopic Management of Digestive Diseases. New Tools and Strategies
Editor	Springer
Editor country	SVIZZERA
Type of publication	Chapter
Authors	M. Campli; A. Cerioli; A. Leppaniemi; A. Arezzo; C. Bergamini
Title	Acute Pancreatitis
Journal	2016
Year of publication	27
Volume	43
pages	Emergency Laparoscopy
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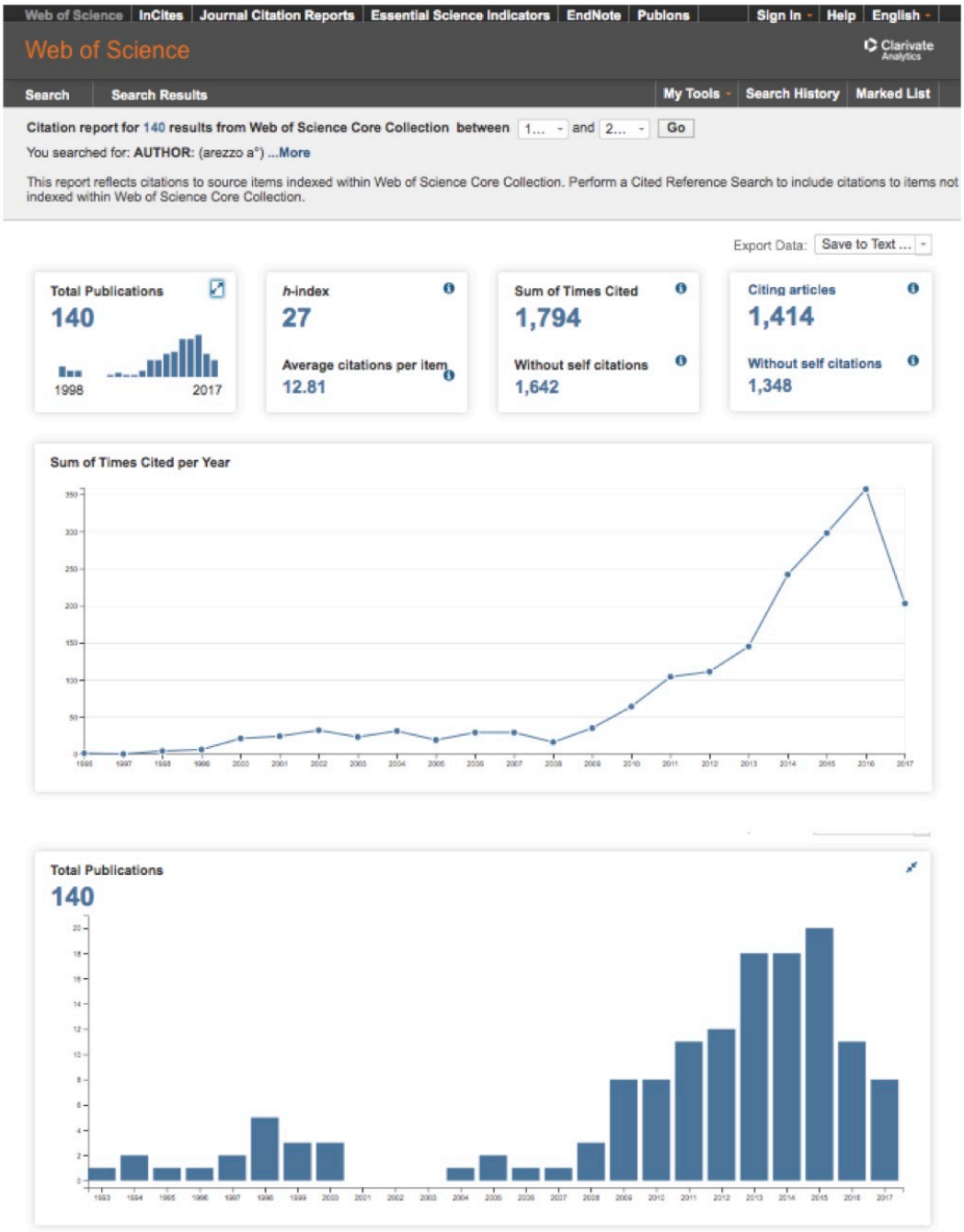
WOS Impact factor	SVIZZERA
Type of publication	Chapter
Authors	Alberto Arezzo; Marco E. Allaix; Mario Campli; Carlo Bergamini; Ferdinando Agresta
Title	Emergency lapararoscopy for colon obstruction and acute diverticulitis
Journal	2016

Year of publication	103
Volume	115
pages	Laparoscopy emergency
	Springer
WOS Impact factor	SVIZZERA
Type of publication	Chapter
Authors	Giovanni Alemanno; Riccardo Somigli; Paolo Prosperi; Mario Campli; Alberto Arezzo; Andrea Valeri; Carlo Bergamini; Mauro Zago
Title	Incarcerated Hernias
Journal	2016
Year of publication	137
Volume	149
pages	Emergency Laparoscopy
	Springer
WOS Impact factor	SVIZZERA
Type of publication	Chapter
Authors	Morino, M.; Arezzo, A.; Famiglietti, F.
Title	Laparoscopic cholecystectomy in cirrhotics
Journal	2015
Year of publication	110
Volume	124
pages	Atlas of laparoscopic Hepato-Pancreato-Biliary Surgery
	Cine-Med, Inc.
WOS Impact factor	STATI UNITI D'AMERICA
Type of publication	Chapter
Authors	A. Trecca; R. Manta; A. Naik; M. De Bellis; A. Arezzo; G. Galloro
Title	Impact of flexible endoscopy in the evaluation of digestive anastomosis
Journal	2014

Year of publication	11
Volume	16
pages	Endoscopic follow-up of digestive anastomosis
	Milano: Springer Verlag Italia
WOS Impact factor	ITALIA
Type of publication	Chapter
Authors	R. Manta; A. Naik; M. Frazzoni; M. Manno; A. Arezzo; M. De Bellis; A. Trecca; G. Bassotti; G. Melotti; R. Conigliano; G. Galloro
Title	Intraoperative endoscopy in the evaluation of digestive anastomoses
Journal	2014
Year of publication	61
Volume	65
pages	Endoscopic follow-up of digestive anastomosis
	Springer Verlag Milan
WOS Impact factor	ITALIA
Type of publication	Chapter
Authors	A. Arezzo; M. Verra; G. Galloro; M. de Bellis; A. Trecca; R. Manta; M. Morino
Title	Review: Therapeutic endoscopy for the treatment of anastomotic dehiscences
Journal	2014
Year of publication	119
Volume	130
pages	Endoscopic Follow-up of Digestive Anastomosis
	Springer Verlag Italia
WOS Impact factor	ITALIA
Type of publication	Chapter
Authors	M. De Bellis; E. Di Girolamo; U. Pace; G. Nasti; M. Claire Tracey; A. Arezzo; R. Manta; A. Trecca; Giuseppe Galloro

Title	Timing and protocols of endoscopic follow-up in operated patients after colorectal surgery
Journal	2014
Year of publication	49
Volume	59
pages	Endoscopic follow-up of digestive anastomosis
	Springer Verlag Milan
WOS Impact factor	ITALIA
Type of publication	Chapter
Authors	M. Morino; A. Arezzo; E. Ruffini; A. Oliaro
Title	Minimally invasive techniques in surgical oncology
Journal	2009
Year of publication	7
Volume	17
pages	New technologies in surgical oncology
	Springer-Verlag
WOS Impact factor	ITALIA
Type of publication	Chapter
Authors	Mario Morino; Alberto Arezzo; E Ruffini; A Oliaro
Title	Tecniche mininvasive in oncologia chirurgica
Journal	2009
Year of publication	7
Volume	18
pages	Nuove tecnologie chirurgiche in oncologia
	Springer
WOS Impact factor	ITALIA
Type of publication	Chapter

Authors	M. Morino; A. Arezzo
Title	Cholecystocholedocholithiasis: Two-stage treatment
Journal	2008
Year of publication	325
Volume	339
pages	Biliary Lithiasis. Basic Science, Current Diagnosis and Management
	Springer
WOS Impact factor	ITALIA
Type of publication	Chapter



Torino, August 31st 2017

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Surg Endosc
DOI 10.1007/s00464-016-5298-7

Multi-port versus single-port cholecystectomy: results of a multi-centre, randomised controlled trial (MUSIC trial)

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Received: 29 July 2016 / Accepted: 14 October 2016

Abstract

Background Single-port laparoscopic surgery as an alternative to conventional laparoscopic cholecystectomy for benign disease has not yet been accepted as a standard procedure. The aim of the multi-port versus single-port cholecystectomy trial was to compare morbidity rates after single-access (SPC) and standard laparoscopy (MPC).

Methods This non-inferiority phase 3 trial was conducted at 20 hospital surgical departments in six countries. At each centre, patients were randomly assigned to undergo either SPC or MPC. The primary outcome was overall morbidity within 60 days after surgery. Analysis was by intention to treat. The study was registered with ClinicalTrials.gov (NCT01104727).

Results The study was conducted between April 2011 and May 2015. A total of 600 patients were randomly assigned to receive either SPC ($n = 297$) or MPC ($n = 303$) and were eligible for data analysis. Postsurgical complications within 60 days were recorded in 13 patients (4.7 %) in the SPC group and in 16 (6.1 %) in the MPC group ($P = 0.468$); however,

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Published online: 24 October 2016

single-access procedures took longer [70 min (range 25–265) vs. 55 min (range 22–185); $P < 0.001$]. There were no significant differences in hospital length of stay or pain VAS scores between the two groups. An incisional hernia developed within 1 year in six patients in the SPC group and in three in the MPC group ($P = 0.331$). Patients were more satisfied with aesthetic results after SPC, whereas surgeons rated the aesthetic results higher after MPC. No difference in quality of life scores, as measured by the gastrointestinal quality of life index at 60 days after surgery, was observed between the two groups. *Conclusions* In selected patients undergoing cholecystectomy for benign gallbladder disease, SPC is non-inferior to MPC in terms of safety but it entails a longer operative time. Possible concerns about a higher risk of incisional hernia following SPC do not appear to be justified. Patient satisfaction with aesthetic results was greater after SPC than after MPC.

Keywords Cholecystectomy · Single port surgery · Randomized controlled trial

In 1992 Pelosi first described the use of a single umbilical puncture for laparoscopic appendectomy [1], and in 1997 Navarra et al. published, as a short note, their results after single-incision laparoscopic cholecystectomy [2]. It is only more recently that the technique has begun to gain wider acceptance. Concerns over the safety issues with this new technique have been voiced by claims that its widespread adoption would lead to a significant increase in complications, especially bile duct injuries, as occurred during the early years of conventional laparoscopic cholecystectomy [3, 4]. More recently published studies have failed to demonstrate any major differences in clinical outcome after the single-incision laparoscopic technique versus standard multi-port laparoscopy [4–9]. Furthermore, there is increasing doubt about whether the new technique actually delivers the benefits of improved aesthetic results, reduced postoperative pain, earlier return to work, and greater patient satisfaction [10–12]. Also, it has been found that a larger peri-umbilical incision and consequent fascial defect may result in a higher rate of incisional hernia.

The aim of this randomised controlled trial (RCT) was to compare overall morbidity after single-incision laparoscopic technique versus standard multi-port laparoscopy for cholecystectomy in terms of skin incision-related morbidity, postoperative pain, and aesthetic results—the potential benefits advocated for single-port laparoscopic surgery.

Methods

We designed this multi-centre RCT under the endorsement of the Technology Committee of the European Association for Endoscopic Surgery (EAES). The project was approved by the local ethical committee (COMITATO ETICO INTERAZIENDALE, A.O.U. CITTA' DELLA SALUTE E DELLA SCIENZA DI TORINO, University of Torino, Italy) of the principle study centre. The project was registered with ClinicalTrials.gov, U.S. International Clinical Trials Databank (U.S. National Institutes of Health), under ID-code NCT01104727, on behalf of the EAES. The study was designed to conform with CONSORT criteria.

Study population

The study population was patients with symptomatic cholelithiasis (gallstones <2 cm in diameter), gallbladder dyskinesia, or gallbladder polyps. Other inclusion criteria were: age 18–75 years, body mass index (BMI) <30, ASA class I–III, absence of non-correctable coagulopathy, and no previous abdominal surgery above the umbilicus. Exclusion criteria were preoperative clinical findings of acute cholecystitis, suspected common bile duct stones or cancer, or previous surgery of the upper abdomen or of the umbilicus.

Patient recruitment

Consecutive eligible patients were recruited at the outpatient clinic of each participating centre by a designated physician. Patients granting informed consent were enrolled in the trial, allocated to one of the treatment groups by computerised randomisation via web-based software, and treated according to the study protocol. Patients unable or refusing to provide informed consent were treated according to current clinical guidelines. Surgeons designated as first operator had to demonstrate documented performance of at least 50 cholecystectomies and previous experience with single-port instruments in at least 15 cases.

Randomisation

Patient data were entered into a web-based database by a designated physician at each centre. Blind computerised randomisation (1:1 allocation ratio), stratified per single centre, was done by unchangeable number-generating software. To ensure that an approximately equal number of patients would be allocated to each arm of the study, each of the 20 centres composing the Consortium had to enrol 30 patients. Patients were allocated to undergo either conventional 4-port cholecystectomy (MPC) or single-port cholecystectomy (SPC).

Operative technique

MPC procedure

A 12-mm Hg pneumoperitoneum was created through either a 10-mm umbilical Hasson's port or a Veress needle,

and a 10-mm umbilical port was inserted; a second 10-mm and two 5-mm ports were then placed. Instrumentation included a straight or angulated laparoscope, laparoscopic graspers, monopolar hook, bipolar forceps, scissors, and a 10-mm clips applier. A plastic bag system for gallbladder extraction was used as needed. Fascia suturing of the 10- and 12-mm access sites was done with resorbable sutures, and the skin was closed with either metallic clips or interrupted sutures.

SPC procedure

A single skin incision was made inside the umbilicus. The subcutaneous tissue was dissected, the muscular fascia exposed and incised along the middle line (linea alba), taking care not to damage the muscular tissue. The peritoneum was identified and incised. A single-port device was inserted and anchored. Depending on which port was used, either straight or curved instruments, crossed or uncrossed handles, gallbladder retractors or transcholecystic sutures or any other technical solution could be employed to complete the procedure safely. After cholecystectomy was completed and the gallbladder removed with/without a plastic bag, the fascia was sutured. Before closure, the fascial defect and the skin incision were measured in maximum length with sterile callipers and each was photographed for documentation. The choice of closure technique was left to the surgeon and had to be specified in detail on the surgical report form. The skin incision was secured with either metallic clips or interrupted sutures.

Primary end point

Overall morbidity rate was defined as any surgery-related morbidity that occurred within 60 days after surgery. Morbidity was defined as the occurrence of any complication directly or indirectly related to surgery. Complications were classified according to Dindo [13].

Secondary end points

Operative time was recorded in minutes between skin incision and end of skin closure. Conversion rate from SPC to MPC was defined as the number of cases in which the procedure was converted from SPC to MPC for safety or technical reasons. Conversion rate to open surgery was defined as the number of cases in which the procedure was converted from SPC or MPC to laparotomy for safety or technical reasons. Postoperative pain was assessed by means of a self-report horizontal visual analogical scale (VAS) for pain recorded daily for the first week and then weekly up to 60 days after surgery. Paracetamol IV 3 times a day was administered for the first 24 h and on demand thereafter. Tramadol was administered when pain control with paracetamol was judged insufficient. A single dose of ketorolac was given on request. Hospital length of stay was defined as the number of inhospital days after surgery. All participating study centres applied the following standardised discharge criteria: normal intake of nutrition; normal mobility; absence of fever (<38 °C); and stable haemoglobin level during postoperative day 1 (<1 g/dL). In cases of same-day discharge from hospital, patients were contacted by telephone the day after the operation. Follow-up examinations were scheduled at 30 and 60 days after surgery. Skin incision-related morbidity was defined as the occurrence of bleeding, infection, necrosis, skin retraction, incisional hernia, or suture dehiscence within 60 days after surgery.

Surgeon-evaluated aesthetic results were judged by three independent surgeons on the basis of a standardised methodology. The surgeons viewed two digital photographs (minimum resolution 800 × 600 pixels) of each patient in standing position taken before and then at 60 days after surgery. One was a close-up photo of the umbilical area and the other a large view of the abdomen. The results were scored on a 5-point Likert scale from 1 to 5 (1 indicates very poor, 2 poor, 3 satisfactory, 4 good, and 5 very good) in answer to the following questions:

1. How would you rate the overall aesthetic results of the abdomen after surgery?
2. How would you rate the scar size?
3. How would you rate the scar shape?
4. How would you rate the skin colour?
5. How would you rate the skin retraction?

Patient-evaluated aesthetic results were judged by the patients on the basis of the scores marked on a 5-point Likert scale administered at the follow-up visit 60 days after surgery in answer to the following questions:

1. How would you rate the overall aesthetic appearance of your body after surgery?
2. How would you rate the impact of the surgical scar/s on the appearance of your abdomen?
3. How would you rate the aesthetic appearance of the surgical scar/s?
4. How would you rate the impact of the surgical scar/s on your everyday life?

Quality of life was assessed with the gastrointestinal quality of life index (GIQLI) at the follow-up visit 60 days after surgery.

Long-term morbidity was defined as any surgery-related morbidity that occurred within 1 year after surgery. Incisional hernia was defined as any fascial defect revealed on

physical examination and confirmed by ultrasound within 1 year after surgery.

Sample size and power calculation

Assuming a baseline overall morbidity rate of 4 % in both the MPC and SPC groups (average morbidity rates drawn from the literature) and considering a clinically significant difference of 4 % (up to 8 % global) for SPC to be non-inferior, with a β-error of 0.2 and α-error of 0.05, a total of 600 patients were needed.

Data analysis

Intra- and postoperative data were entered in the web-based database at any time during the study by the recruiting surgeon. The photographic documentation was also uploaded into the computerised database. Patients' personal data were protected against unauthorised or accidental access. All analyses were carried out primarily on an intention-to-treat basis. Risk of bias was evaluated based on the CONSORT 2010 [14] statement.

Monitoring

Three experts in bilio-pancreatic and laparoscopic surgery were designated as members of multi-port versus single-port cholecystectomy (MUSIC) trial monitoring committee (Music TMC). They had access to the data during the entire course of the study and could recommend cessation of the trial if one arm was providing manifestly inferior results.

Statistical analysis

Categorical variables are described as frequencies and percentages and continuous variables as the median. The interquartile range (IQR) is given in brackets. The association between any categorical variable and treatment arm (MPC/SPC) was analysed using Fisher's exact test; the Mann–Whitney test was used for continuous variables. All reported *P* values were obtained by the two-sided exact method at the conventional 5 % significance level. Data were analysed as of June 2016 by R 3.2.3 (R Foundation for Statistical Computing, Vienna-A, http://www.R-project.org).

Results

Following Ethical Committee approval, enrolment was begun on 1 April, 2011 and closed on 7 July, 2015. All 20 centres but 1 involved in the study at the time of trial registration recruited patients. Six of these 19 centres recruited an insufficient number of patients to complete the series according to local stratification (Table 1). By unanimous decision of the Consortium, the number of patients to be enrolled and randomised at the 13 other centres was raised to 40 in order to achieve the target of 600 patients (Fig. 1). The data from the patients recruited at the six centres were pooled as a miscellaneous group for sensitivity analysis by centre.

The indication for cholecystectomy was cholelithiasis in 578 patients, gallbladder polyps in 20, and gallbladder dyskinesia in 2. Table 2 presents the patients' characteristics, Table 3 the definitive diagnosis, and Table 4 the various device systems.

Data regarding skin and fascial incisions were reported in 278/297 patients. The median size of the skin incision was 25 mm (range 20–30). The median size of the fascial incision was 25 mm (range 20–30). Intraoperative complications were recorded in 25 patients in the MPC group (gallbladder perforation in 20, liver laceration in 3, and bleeding in 2) and in 21 patients in the SPC group (gallbladder perforation in 14, duodenal injury in 1, liver laceration in 1, and bleeding in 5) ($P = 0.647$). During SPC, an additional trocar was added in 18 procedures, and more than one trocar in 14 procedures, which were then recorded as conversion to laparoscopy. One procedure in the SPC group was converted to open surgery. Approximately equal amounts of analgesia were recorded for both groups (Table 5). The median VAS pain score was 2 in the MPC group (range 1–4) and 3 in the SPC group (range 1–4) ($P = 0.905$). The median hospital length of stay was 2 days in the MPC group (range 1–3) and 3 days in the SPC group (range 1–2) ($P = 0.808$). Postoperative complications during inhospital stay were recorded in 3 patients in the MPC group (biliary leak in 1, pulmonary effusion in 1, and subcutaneous emphysema in 1) and in 5 in the SPC group (bleeding in 2, hyperthermia in 1, increase in inflammatory markers in 1, and acute hypertension in 1) ($P = 0.496$).

A total of 541/600 patients (90.2 %) completed follow-up at 60 days. Postoperative complications at 60 days occurred in 11 MPC group patients (biliary leak in 1, skin suture dehiscence in 4, fascial suture dehiscence in 2, hyperthermia in 1, pulmonary infection in 1, diarrhoea in 1, and subphrenic abscess in 1) and in 11 SPC group patients (biliary leak in 2, skin suture dehiscence in 2, fascial suture dehiscence in 5, intra-abdominal collection in 1, and persistent neck pain in 1) ($P = 1.000$). Postoperative complications within 60 days were recorded in 13 patients (4.7 %) in the MPC group and in 16 (6.1 %) in the SPC group, which demonstrated the non-inferiority of the SPC technique as compared to MPC in terms of morbidity ($P = 0.468$). Complications recorded in 541/600 patients

Table 1 Number of patients treated at each study centre

	MPC	SPC	Total
University of Torino, Turin, Italy	21	21	42
University of Torino (2nd centre), Turin, Italy	22	21	43
Humanitas, Rozzano, Italy	21	20	41
A.V. Vishnevsky, Moscow, Russia	20	21	41
Hadassah-Hebrew University Medical Centre, Jerusalem, Israel	20	21	41
University Hospital G. Martino, Messina, Italy	20	20	40
University of Insubria, Varese, Italy	21	21	42
University of Roma Tor Vergata, Rome, Italy	21	21	42
University of San Luigi Gonzaga, Orbassano (TO), Italy	20	19	39
Hospital Latisana, Italy	21	21	42
University of Graz, Austria	20	18	38
University of Bremen, Germany	23	18	41
Moscow Clinical Scientific Centre, Moscow, Russia	21	21	42
Esther Koplowitz Centre, Barcelona, Spain	16	12	28
Hospital Bolzano, Italy	12	10	22
Institute of Chemical Biology and Fundamental Medicine, Novosibirsk, Russia	1	5	6
Niguarda CàGranda Hospital, Milan, Italy	1	3	4
Bilim University of Istanbul, Turkey	2	2	4
University Hospital Valld' Hebron, Barcelona, Spain	0	2	2
Total no./total no. of enrolled and randomised patients in each treatment arm	303	297	600

MPC multi-port cholecystectomy, *SPC* single-port cholecystectomy

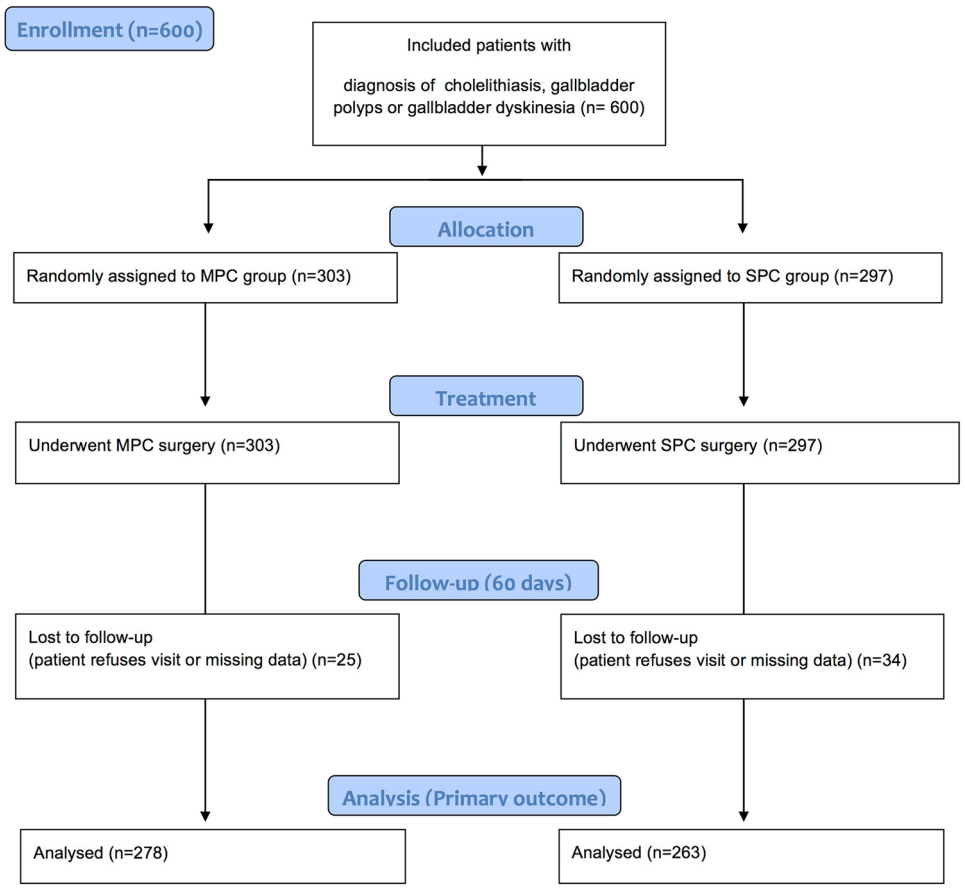

Fig. 1 CONSORT 2010 flow diagram

Table 2 Patients' characteristics

	MPC group					SPC group					*P* value
	Min	25th IQR	Median	75th IQR	Max	Min	25th IQR	Median	75th IQR	Max	
Age (years)	18	39	48	60	86	20	37	47	59	85	0.292
Weight (kg)	46	60	70	78	105	43	60	70	80	116	0.667
Height (cm)	142	162	167	172	197	126	160	167	175	195	0.873
BMI (kg/m^2)	18.0	22.8	24.6	27.1	38.5	17.2	22.7	24.9	27.7	40.1	0.598

MPC multi-port cholecystectomy, *SPC* single-port cholecystectomy, *IQR* interquartile range

Table 3 Definitive diagnosis of gallbladder disease

	MPC group	SPC group	Total
Cholelithiasis	285	278	563
Gallbladder polyps	9	11	20
Cholelithiasis + cholecystitis	4	4	8
Cholelithiasis + gallbladder empyema	2	1	3
Cholelithiasis + umbilical hernia	0	2	2
Gallbladder dyskinesia	2	0	2
Cystic duct obstruction	0	1	1
Choledocholithiasis	1	0	1

MPC multi-port cholecystectomy, *SPC* single-port cholecystectomy

Table 4 Number of single-port instruments by trademark name and manufacturer

Instrument (manufacturer)	No.
SILS Port® (Covidien)	74
XCone® (Karl Storz)	58
TriPort/Plus® (Olympus)	51
Octoport® (Dalimsurg)	27
GelPoint® (Applied Medical)	21
Endocone® (Karl Storz)	21
SSL® (Ethicon)	19
S-Portal® (Karl Storz)	4
Key Port® (Richard Wolf)	1

were classified according to Dindo [13] (Table 6). No further surgery was required in any cases.

A total of 446/600 patients (74.3 %) completed follow-up at 1 year. Postoperative complications were recorded in 9 MPC group patients (biliary stenosis in 1, skin retraction in 2, keloid formation in 3, and incisional hernia in 3) and in 10 SPC group patients (biliary stenosis in 1, skin retraction in 2, keloid formation in 1, and incisional hernia in 6) ($P = 0.817$). Complications within 1 year after surgery were recorded in 22 patients (9.7 %) in each group ($P = 1.000$).

Data on patient-evaluated aesthetic results were available for 513/600 patients. The patients in the SPC group gave the aesthetic results a significantly higher score on all accounts (Table 7). Data on surgeon-evaluated aesthetic result were available for 289/600 patients. The surgeons gave significantly higher scores particularly for scar and skin retraction in the MPC group (Table 8). There were no significant differences between the two groups (505/600 patients) in quality of life scores as measured with the GIQLI at 60 days after surgery (Table 9).

Discussion

Although single-port laparoscopic surgery is not new [1, 2], its use has gained momentum over the last few years in part through the support of major surgical instrument manufacturers. This raises concerns about a possible industry-driven interest in promoting wider use of the technique. There is no doubt, however, that single-port surgery has several drawbacks particularly in relation to the lack of "triangulation" to which laparoscopic surgeons have grown accustomed in terms of both instruments and scope. Although this seems to have been overcome by the growing acceptability of in-line viewing, device manufacturers have focused their product research on developing and marketing a variety of curved instruments featuring

Table 5 Postoperative analgesic consumption

	Tramadol	Paracetamol	Paracetamol codein	Ketorolac
First 6 h				
Multi-port group	87	212	2	96
P value	0.109	0.298	1.000	0.365
Single-port group	103	195	2	83
6 h—1st day				
Multi-port group	39	222	7	70
P value	0.479	0.919	0.545	1.000
Single-port group	44	215	4	69
2nd day				
Multi-port group	6	119	6	27
P value	0.226	0.932	0.123	0.658
Single-port group	11	115	1	23
First week				
Multi-port group	7	68	2	13
P value	0.799	0.310	1.000	0.836
Single-port group	8	56	1	11

Table 6 Postoperative complications within 60 days graded according to Dindo–Clavien

	MPC	SPC
Grade I	9	10
Grade II	1	1
Grade IIIa	3	5
Grade IIIb	0	0
Grade IVa	0	0
Grade IVb	0	0
Grade V	0	0

P value = 0.865

MPC multi-port cholecystectomy, *SPC* single-port cholecystectomy

Table 7 Patient-evaluated scoring of aesthetic results in response to four question items

Score	Q1		Q2		Q3		Q4	
	MPC	SPC	MPC	SPC	MPC	SPC	MPC	SPC
1	1	0	7	1	3	0	12	8
2	1	3	5	5	5	3	3	6
3	30	10	42	14	32	11	26	13
4	106	55	96	60	94	67	97	68
5	131	176	119	164	135	163	131	149
P value	<0.001		<0.001		<0.001		0.025	

5-point Likert scale from 1 (poor) to 5 (very good)

1. How would you rate the overall aesthetic appearance of your body after surgery?

2. How would you rate the impact of surgical scar(s) on the image of your abdomen?

3. How would you rate the aesthetic appearance of the surgical scar(s)?

4. How would you rate the impact of the surgical scar(s) on your everyday life?

MPC multi-port cholecystectomy, *SPC* single-port cholecystectomy

different characteristics with the aim of restoring standard triangulation as provided in a laparoscopic environment. Nevertheless, a recent study that measured ergonomic performance on a virtual-reality simulator designed for the purpose demonstrated that, after a short learning curve, only very experienced surgeons were able to perform the surgical tasks safely and effectively, while all the other surgeons found technique acquisition to be challenging [15].

For this reason, we chose as the main outcome the non-inferiority of SPC versus MPC in terms of overall post-operative morbidity at 60 days, and the results confirm this: no difference in severity of complications was observed. Hence, the hypothesis that SPC would be associated with a higher complications rate, but with greater overall satisfaction with clinical and aesthetic results, is not confirmed [6]. Few patients experienced complications, mostly minor, with 2 cases of biliary leak and 1 case of biliary stenosis recorded per group, all successfully treated by endoscopic retrograde cholangio-pancreatography (ERCP). Operative time was slightly but significantly longer in the SPC group, although this difference seems of marginal relevance for operating room organisation. An additional trocar was employed in very few cases, and in even fewer in which the procedure was converted to laparoscopy.

Moreover, it has been claimed that a larger peri-umbilical incision and consequent fascial defect would increase

Table 8 Surgeon-evaluated scoring of aesthetic results in response to five question items

Scores	Q1		Q2		Q3		Q4		Q5	
	MPC	SPC	MPC	SPC	MPC	SPC	MPC	SPC	MPC	SPC
1	0	0	0	0	0	0	0	0	0	0
2	3	2	2	1	2	3	0	0	6	2
3	10	19	8	19	8	25	27	32	14	36
4	78	68	77	68	80	61	69	59	75	55
5	56	53	60	54	57	53	51	51	52	49
P value	0.293		0.113		0.007		0.574		0.001	

5-point Likert scale from 1 (poor) to 5 (very good)

1 = How would you rate the overall aesthetic appearance of patient's abdomen after surgery?

2 = How would you rate the scar(s) size?

3 = How would you rate the scar(s) shape?

4 = How would you rate the skin colour?

5 = How would you rate the skin retraction?

MPC multi-port cholecystectomy, *SPC* single-port cholecystectomy

Table 9 Gastrointestinal quality of life index (GIQLI) scores

	MPC group					SPC group					*P* value
	Min	25th IQR	Median	75th IQR	Max	Min	25th IQR	Median	75th IQR	Max	
GIQLI_sum	25	114	122	128	140	44	117	123	129	144	0.124
GIQLI_phy	3	33	35	36	44	15	33	35	36	44	0.684
GIQLI_bow	6	21	23	24	24	8	21	23	24	24	0.246
GIQLI_emo	6	23	26	28	32	6	24	26	28	32	0.111
GIQLI_ugi	3	26	28	30	32	7	27	29	31	32	0.216
GIQLI_met	3	10	11	12	12	2	10	11	12	12	0.020

GIQLI subscale division

GIQLI_sum: all items, 1–36

GIQLI_phy (physical role): item 1, 18, 19, 20, 21, 22, 23, 24, 25, 26, 29

GIQLI_bow (large bowel function): item 6, 7, 30, 31, 34, 36

GIQLI_emo (emotional role): item 8, 10, 11, 12, 13, 14, 15, 16

GIQLI_ugi (upper GI tract function): item 4, 9, 17, 27, 28, 32, 33, 35

GIQLI_met (meteorism): item 3, 4, 5

MPC multi-port cholecystectomy, *SPC* single-port cholecystectomy, *IQR* interquartile range

the risk of incisional hernia [9]. This article presents the largest series with 1-year follow-up of patients enrolled in a single-blind, multi-centre, prospective, randomised, controlled trial of SPC versus standard MPC. Although this was true in our series, the incidence of incision hernia was so low in both groups that many more cases would be needed to achieve significance if confirmed. This reinforces the hypothesis that the finding of Marks et al. [9] was depending on an increased rate of incisional adverse events, in particular a higher rate of superficial wound complications in the single-port group. This was not confirmed in our series, three times larger, and in which possible local biases were more likely to be avoided due to the proportional distribution of patients among the different centres. No other significant differences between the groups were observed in relation to the perioperative course, pain VAS scores, analgesic consumption, or QoL at 60 days as assessed by the GIQLI.

The basic rationale for the interest in single-port laparoscopy is that, because it may improve cosmesis and decrease postoperative pain, patient satisfaction would be greater than after standard laparoscopy. Our study shows that the majority of the patients in the single-port group were pleased with their aesthetic results, although it may be argued that other not investigated factors might have influenced their personal opinion. In contrast, the surgeon-evaluated aesthetic results were based on a comparative, standardised methodology in which the images were

viewed and objectively scored by three independent surgeons. In their opinion, the scar shape and skin retraction after MPC appeared aesthetically more acceptable.

There are several limitations to this study that must be discussed. First, approximately 25 % of patients were lost to follow-up at 1 year, which is higher than would be normally expected for a 12-month prospective study. Second, all surgeons participating in this trial had performed at least 15 previous SPC cases, but the ability to generalise outcomes from this study might not be applicable to those in the initial learning curve associated with this new technique. Finally, the follow-up of 12 months might be too short to determine the true differences between SPC and MPC in terms of risk for hernia development.

Conclusions

In selected patients undergoing cholecystectomy for benign gallbladder disease, a single-access technique is non-inferior to standard laparoscopy in terms of safety, but it entails a longer operative time. The short follow-up cannot exclude possible concerns about a higher risk of incisional hernia following SPC, although this was not demonstrated in the present study. Patients rated the aesthetic results after the single-access technique higher than after standard laparoscopy.

Acknowledgments The study was supported by a research grant from the European Association for Endoscopic Surgery in 2011.

Compliance with ethical standards

Disclosures Dr. Alberto Arezzo reports having received a grant from the European Association for Endoscopic Surgery to conduct this study. Dr. Luigi Boni reports having received travel grants from Karl Storz during this study. Drs. Roberto Passera, Alberto Bullano, Yoav Mintz, Asaf Kedar, Elisa Cassinotti, Riccardo Rosati, Uberto Fumagalli Romario, Mario Sorrentino, Marco Brizzolari, Nicola Di Lorenzo, Achille Lucio Gaspari, Dario Andreone, Elena De Stefani, Giuseppe Navarra, Salvatore Lazzara, Maurizio Degiuli, Kirill Shishin, Igor Khatkov, Ivan Kazakov, Rudolf Schrittwieser, Thomas Carus, Alessio Corradi, Guenther Sitzman, Antonio Lacy, Selman Uranues, Amir Szold, and Mario Morino have no conflicts of interest or financial ties to disclose.

References

1. Pelosi MA, Pelosi MA III (1992) Laparoscopic appendectomy using a single umbilical puncture (minilaparoscopy). J Reprod Med 37:588–594
2. Navarra G, Pozza E, Occhionorelli S, Carcoforo P, Donini I (1997) One-wound laparoscopic cholecystectomy. Br J Surg 84:695
3. Allemann P, Schafer M, Demartines N (2010) Critical appraisal of single port access cholecystectomy. Br J Surg 97:1476–1480
4. Joseph M, Phillips MR, Farrell TM, Rupp CC (2012) Single incision laparoscopic cholecystectomy is associated with a higher bile duct injury rate. A review and a word of caution. Ann Surg 256:1195–1200
5. Asakuma M, Hayashi M, Komeda K, Shimizu T, Hirokawa F, Miyamoto Y, Okuda J, Tanigawa N (2011) Impact of single-port cholecystectomy on postoperative pain. Br J Surg 98:991–995
6. Ma J, Cassera MA, Spaun GO, Hammill CW, Hansen PD, Aliabadi-Wahle S (2011) Randomized controlled trial comparing single-port laparoscopic cholecystectomy and four-port laparoscopic cholecystectomy. Ann Surg 254:22–27
7. Lee PC, Lo C, Lai PS, Chang JJ, Huang SJ, Lin MT, Lee PH (2010) Randomized clinical trial of single-incision laparoscopic cholecystectomy versus minilaparoscopic cholecystectomy. Br J Surg 97:1007–1012
8. Lirici MM, Califano AD, Angelini P, Corcione F (2011) Laparoendoscopic single site cholecystectomy versus standard laparoscopic cholecystectomy: results of a pilot randomized trial. Am J Surg 202:45–52
9. Marks JM, Phillips MS, Tacchino R, Roberts K, Onders R, DeNoto G, Gecelter G, Rubach E, Rivas H, Islam A, Soper N, Paraskeva P, Rosemurgy A, Ross S, Shah S (2013) Single-incision laparoscopic cholecystectomy is associated with improved cosmesis scoring at the cost of significantly higher hernia rates: 1-year results of a prospective randomized, multicenter, single-blinded trial of traditional multiport laparoscopic cholecystectomy vs single-incision laparoscopic cholecystectomy. J Am Coll Surg 216:1037–1047
10. Edwards C, Bradshaw A, Ahearne P, Dematos P, Humble T, Johnson R, Mauterer D, Soosaar P (2010) Single-incision laparoscopic cholecystectomy is feasible: initial experience with 80 cases. Surg Endosc 24:2241–2247
11. Vettoretto N, Arezzo A (2010) Human natural orifice translumenal endoscopic surgery: on the way to two different philosophies? Surg Endosc 24:490–492
12. Lirici MM, Arezzo A (2006) Surgery without scars: the new frontier of minimally invasive surgery? Controversies, concerns and expectations in advanced operative endoscopy. Minim Invasive Ther Allied Technol 15:323–324
13. Moher D, Hopewell S (2010) CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. BMJ 340:c869
14. Dindo D, Demartines N, Clavien PA (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240:205–213
15. Rimonda R, Brown S, Tang B, Cuschieri A (2012) Ergonomic performance with crossed and uncrossed instruments in single port laparoscopic surgery. Surg Endosc 26:3605–3611

Surg Endosc (2014) 28:427–438
DOI 10.1007/s00464-013-3238-3

Systematic review and meta-analysis of endoscopic submucosal dissection versus transanal endoscopic microsurgery for large noninvasive rectal lesions

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Received: 27 May 2013 / Accepted: 23 September 2013 / Published online: 23 October 2013

Abstract
Background For almost 30 years, transanal endoscopic microsurgery (TEM) has been the mainstay treatment for large rectal lesions. With the advent of endoscopic submucosal dissection (ESD), flexible endoscopy has aimed at en bloc R0 resection of superficial lesions of the digestive tract. This systematic review and meta-analysis compared the safety and effectiveness of ESD and full-thickness rectal wall excision by TEM in the treatment of large nonpedunculated rectal lesions preoperatively assessed as noninvasive.
Methods A systematic review of the literature published between 1984 and 2010 was conducted (Registration no. CRD42012001882). Data were integrated with those from the original databases requested from the study authors when needed. Pooled estimates of the proportions of patients with en bloc R0 resection, complications, recurrence, and need for further treatment in the ESD and TEM series were compared using random-effects single-arm meta-analysis.
Results This review included 11 ESD and 10 TEM series (2,077 patients). The en bloc resection rate was 87.8 % (95 % confidence interval [CI] 84.3–90.6) for the ESD patients versus 98.7 % (95 % CI 97.4–99.3 %) for the TEM patients ($P < 0.001$). The R0 resection rate was 74.6 % (95 % CI 70.4–78.4 %) for the ESD patients versus 88.5 % (95 % CI 85.9–90.6 %) for the TEM patients ($P < 0.001$). The postoperative complications rate was 8.0 % (95 %, CI

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5.4–11.8 %) for the ESD patients versus 8.4 % (95 % CI 5.2–13.4 %) for the TEM patients ($P = 0.874$). The recurrence rate was 2.6 % (95 % CI 1.3–5.2 %) for the ESD patients versus 5.2 % (95 % CI 4.0–6.9 %) for the TEM patients ($P < 0.001$). Nevertheless, the rate for the overall need of further abdominal treatment, defined as any type of surgery performed through an abdominal access, including both complications and pathology indications, was 8.4 % (95 % CI 4.9–13.9 %) for the ESD patients versus 1.8 % (95 % CI 0.8–3.7 %) for the TEM patients ($P < 0.001$).
Conclusions The ESD procedure appears to be a safe technique, but TEM achieves a higher R0 resection rate when performed in full-thickness fashion, significantly reducing the need for further abdominal treatment.

Keywords Rectal adenoma · Transanal endoscopic microsurgery · Endoscopic submucosal dissection · Systematic review · Meta-analysis

For nearly 30 years, transanal endoscopic microsurgery (TEM) has been the optimal mainstay treatment for large rectal lesions. Initially conceived for treating benign lesions, its indications were extended to early rectal cancer treatment when Hermanek and Gall [1] assessed criteria to determine lesions at "low risk" for recurrence. One increasingly recognized advantage of the technique versus standard transanal surgery is the high rate of en bloc resection with disease-free margins, which is strictly related to the risk of recurrence [2].

With the advent of endoscopic submucosal dissection (ESD) about 10 years ago, flexible endoscopy permitted a surgical-like technique for en bloc resection of superficial lesions of the digestive tract. First indicated for the upper gastrointestinal tract [3], ESD then was applied to the lower gastrointestinal tract with promising results [4]. Although ESD represents an alternative to endoscopic mucosal resection (EMR) of the colon, its application to the rectum can be compared with TEM, both aiming to achieve en bloc R0 excision.

This study aimed to evaluate in a systematic review and meta-analysis whether ESD has clinically relevant short-term advantages in terms of safety and effectiveness compared with TEM in the treatment of large nonpedunculated rectal lesions preoperatively assessed as noninvasive.

Methods

The methods for the analysis and generation of inclusion criteria were based on the Cochrane Collaboration guidelines [5] and the PRISMA recommendations [6]. According to population, interventions, comparators, outcome measures, and setting (PICOS) criteria, patients were included if they had large nonpedunculated rectal lesions preoperatively assessed as noninvasive for which either TEM or ESD was indicated. The study methods were documented in a protocol registered and accessible at http://www.crd.york.ac.uk/prospero/ (Registration no. CRD42012001882).

Criteria for identifying studies and eligibility

The study aimed to include randomized or quasi-randomized studies that directly compared TEM and ESD. Because we knew and verified that similar studies were not available, we included prospective series that examined one of the two treatments provided they had the same inclusion and exclusion criteria. To be eligible, studies had to include reports on patients with a large (>2 cm) nonpedunculated rectal lesion preoperatively assessed as noninvasive by digital examination and/or endoscopic ultrasound (EUS) (confined to the mucosal layer) or lesions treated endoscopically by the ability to be lifted when the submucosal layer was injected below the lesion.

The exclusion criteria ruled out preoperative biopsies positive for invasive malignancy when available, TEM performed in a non-full-thickness fashion, and the impossibility to hive-off data from mixed series. Also excluded were studies reporting data on colon and rectal lesions that could not be broken up.

The criteria required that TEM had been performed in full-thickness fashion according to the technique described by Buess et al. [7]. When the technique was not specified, the authors were contacted for confirmation. Articles were included if a submucosal dissection was performed by TEM only for those lesions at risk for peritoneal opening. The criteria required that ESD had been performed after submucosal injection and lifting by any of the techniques described in the literature, including the different knives available.

Because most of the ESD series merged data on colonic and rectal lesions in a way that the two types could not be distinguished, the authors were contacted to provide a database of their published series restricted to rectal lesions only. Rectal lesions were defined as any lesion with an upper margin located within 18 cm of the anal verge, which was assessed by means of rigid rectoscopy in the TEM series and by flexible endoscopy in the ESD series.

End points

The primary end point of this review was effectiveness of resection (i.e., en bloc resection rate, defined as the rate of lesions excised in a single specimen, and R0 resection rate,

defined as the rate of lesions excised with margins free of disease) as assessed by the pathologist. The secondary end points were size of the lesions excised, time for completion of the procedure, safety (i.e., postprocedural complications such as bleeding and perforation and the need for abdominal surgery to manage complications), recurrence rate as assessed by a minimum of 6 months follow-up evaluation, the need for abdominal surgery for oncologic reasons, and finally the overall need for abdominal surgery. Abdominal surgery was defined as any type of surgery performed through an abdominal access.

Search strategy

Searches of the published literature were conducted for the period between January 1984 and December 2010. Only articles published in English or German were included. Studies were identified by electronic searches of Pubmed and EMBASE.

The following strategy was used to search both PubMed and EMBASE at a single time during January 2011: endoscopic AND submucosal AND resection* OR (endoscopic AND submucosal AND dissection*) OR (endoscopic AND submucosal AND excision*) OR (endoscopic AND mucosal AND resection*) OR (endoscopic AND resection*) OR (endoscopic AND excision*) OR (endoscopic AND mucosal AND excision*) OR (endoscopic AND treatment*) OR (endoscopic AND therapy*) OR (rectoscopic AND mucosal AND resection*) OR (rectoscopic AND resection*) OR (rectoscopic AND excision*) OR (rectoscopic AND mucosal AND excision*) OR (rectoscopic AND treatment*) OR (rectoscopic AND therapy*) OR (colonoscopic AND mucosal AND excision*) OR (colonoscopic AND resection*) OR (colonoscopic AND excision*) OR (colonoscopic AND treatment*) OR (colonoscopic AND therapy*) AND (colorectal AND 'neoplasms'/exp OR (colorectal AND tumor*) OR (colorectal AND tumour*) OR (colorectal AND neoplasm*) OR ('rectal'/exp AND neoplasm*) OR ('adenoma'/exp AND ('rectum'/exp OR 'rectal'/exp OR colorectal))) OR (tem OR (transanal AND endoscopic AND 'microsurgery'/exp) AND 'surgery'/exp OR transanal OR peranal AND (colorectal AND 'neoplasms'/exp OR (colorectal AND tumor*) OR (colorectal AND tumour*) OR (colorectal AND neoplasm*) OR ('rectal'/exp AND neoplasm*) OR ('adenoma'/exp AND ('rectum'/exp OR 'rectal'/exp OR colorectal)))) AND 'rectal'/exp AND 'neoplasm'/exp AND ('endoscopy'/exp OR endoscopic OR 'microsurgery'/exp OR transanal OR mucosal OR 'resection'/exp) OR (endoscopic AND mucosal AND 'resection'/exp) OR (endoscopic AND submucosal AND 'dissection'/exp) AND [1984-2010]/py.

Study selection

Titles were screened by two authors (A.A. and M.V.) to exclude nonrelated publications. Studies were excluded if the interventions, as reported in the abstracts, clearly differed from ESD or TEM or did not focus on the colorectal area.

The full text of the remaining articles was read to determine whether they were eligible for inclusion in the review. Studies were excluded in which preoperatively assessed rectal cancers were treated. When the same data of a single research group were reported in multiple publications, only the study reporting on the largest cohort was included.

Data extraction was independently performed by the two reviewers using predefined data extraction forms. A third investigator (M.M.) arbitrated in the event that agreement was not reached.

From each report, the reviewers independently collected the following data when available: year of publication, prospective or retrospective study design, enrollment period, number of patients included, mean age, gender distribution, lesion location (colon/rectum), Kudo pit-pattern classification [8], EUS, type of device used, mean operating time, mean tumor size, complication rate, rate of surgery due to complications, histology (adenoma, carcinoma in situ, invasive cancer, carcinoid), rate of histologically verified en bloc resection, rate of histologically verified complete resection (R0), rate of surgery for oncologic reasons, follow-up evaluation, histologically demonstrated recurrence, and need of further treatment for disease recurrence.

Quality assessment

All the studies fulfilling the selection criteria for this review were assessed to determine methodologic quality and risk of bias. The following quality items were scored: study design, sequence generation, cohort size, lesion type before intervention, lesion size, incidence of invasive carcinomas at final histology, length of the follow-up period, and objective definition of outcome parameters (complications and recurrence).

Table 1 reports the individual scores of quality assessment items per study. Because the data on colonic and rectal lesions from most of the ESD series were merged in such a way that they could not be distinguished, the authors were asked to provide a database of their published series restricted to rectal lesions only.

Statistical analysis

All analyses were performed according to the original treatment allocation (intention-to-treat analysis). Fixed- and

Table 1 Individual scores of quality assessment items per study

Author	Year	Intervention	Study characteristics			Tumor characteristics	Outcome assessment: safety		Outcome assessment: effectiveness	
			n	Study design	Consecutive series	Mean (±SD) size of lesions (mm)	Complications reported	Objective definition of complication	Recurrences reported	Objective definition of recurrence
Fujishiro et al. [11]	2006	ESD	35	Unclear	Yes	26.2 ± 14.0	Yes	No	Yes	No
Onozato et al. [12]	2007	ESD	30	Retrospective	Yes	32.8 ± NA	Yes	No	Yes	No
Ohya et al. [13]	2009	ESD	45	Unclear	Yes	35.0 ± NA	Yes	No	No	No
Iizuka et al. [14]	2009	ESD	26	Retrospective	Unclear	36.0 ± 20.0	Yes	No	No	No
Uraoka et al. [15]	2010	ESD	37	Retrospective	Yes	NA	Yes	No	No	No
Ishii et al. [16]	2010	ESD	9	Retrospective	Unclear	34.0 ± 16.0	Yes	No	Yes	Yes
Takeuchi et al. [17]	2010	ESD	14	Prospective	Unclear	28.7 ± NA	Yes	No	No	No
Yoshida et al. [18]	2010	ESD	110	Unclear	Unclear	29.1 ± NA	Yes	No	No	No
Saito et al. [19]	2010	ESD	158	Prospective	Yes	35.0 ± 18.0	Yes	No	No	No
Fusaroli et al. [20]	2009	ESD	8	Unclear	Unclear	41.9 ± NA	Yes	No	No	No
Niimi et al. [21]	2010	ESD	64	Retrospective	Yes	28.9 ± NA	Yes	No	No	No
Said and Stippel [22]	1996	TEM	260	Retrospective	No	NA	Yes	No	Yes	Yes
Cocilovo et al. [23]	2003	TEM	56	Prospective	Unclear	49.0 ± 22.8	Yes	No	Yes	No
Langer et al. [24]	2003	TEM	79	Retrospective	No	33.0 ± 15.0	Yes	No	Yes	No
Neary et al. [25]	2003	TEM	21	Prospective	Yes	39.0 ± 26.0	Yes	No	Yes	No
Schafer et al. [26]	2006	TEM	33	Retrospective	Unclear	91.2 ± 22.8	Yes	No	Yes	No
Ganai et al. [27]	2006	TEM	134	Retrospective	Unclear	31.0 ± 14.0	Yes	No	Yes	Yes
Doornebosch et al. [28]	2008	TEM	47	Prospective	Yes	44.7 ± 13.3	Yes	Unclear	Yes	No
Guerrieri et al. [29]	2010	TEM	402	Retrospective	Unclear	NA	Yes	No	Yes	No
De Graaf et al. [30]	2011	TEM	216	Prospective	Unclear	30.0 ± NA	Yes	No	Yes	Yes
Morino et al. [31]	2011	TEM	293	Prospective	Unclear	50.0 ± NA	Yes	No	Yes	No

ESD endoscopic submucosal dissection, *NA* not available, *TEM* transanal endoscopic microsurgery

random-effects meta-analyses of studies reporting single proportions were used to calculate an overall proportion. Because all the studies reported the results of only one technique in a series of patients, the logit transformed proportion of patients with recurrence or complication was used as the outcome parameter in the meta-analysis. We added 0.5 to all the cell frequencies of studies with a zero cell count.

Particularly, the random-effects model incorporates any remaining variability beyond chance that exists among studies, taking into account differences in sample size whereby proportions have been measured in each trial. This within-study variation was accounted for by using the exact binomial distribution. Individual and pooled estimates of these proportions together with 95 % confidence intervals (95 % CI) on recurrence and complication rates then were presented in the forest plots.

Operating time and tumor size were compared using their reported means and standard deviations (SDs). When means and/or SDs were not reported, they were estimated from the reported medians and ranges using the Hozo et al. [9] approach.

Potential sources of heterogeneity were explored in three different sensitivity analyses: fixed versus random-effects models (with the second model incorporating heterogeneity), cumulative meta-analysis (sequential inclusion of studies by date of publication), and influence meta-analysis (calculation of pooled estimates with omission of one study at a time).

All analyses were performed using R 2.15.0 and Meta-analyst 3.13 (for continuous outcomes) (R Foundation for Statistical Computing, Vienna, Austria) [10].

Results

The search retrieved 9,315 studies. The selection procedure is illustrated in Fig. 1. Of the 9,315 studies, 57 were

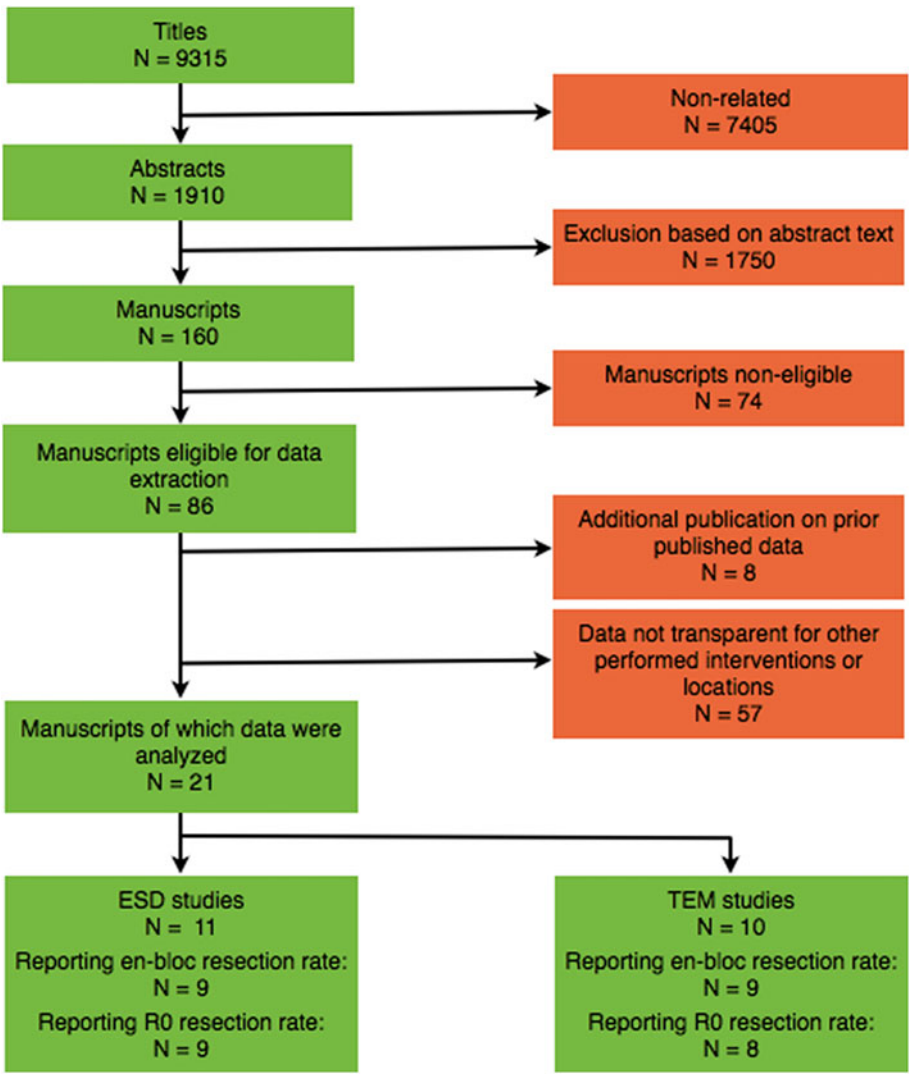

Fig. 1 Flow chart diagram of the systematic search and study selection strategy

excluded because it was unclear whether full-thickness TEM procedures were performed and whether an ESD procedure was performed to treat colonic or rectal lesions. We were unable to clarify these doubts because we received no reply to our request from the respective study authors. In all, 21 studies met the inclusion criteria for a total of 2,077 patients: 11 ESD series [11–21] totaling 536 patients, and 10 TEM series [2, 22–30], totaling 1,541 patients.

The mean polyp size was 35 mm (95 % CI 31–39 mm) in the ESD series versus 40 mm (95 % CI 29–51 mm) in the TEM series ($P = 0.393$). The operating time was 96 min (95 % CI 84–107 min) in the ESD series versus 67 min (95 % CI 53–82 min) in the TEM series ($P = 0.003$).

En bloc and RO resection

The en bloc resection rate was available for 9 ESD and 9 TEM series. The pooled estimate of the proportion of patients was 87.8 % (95 % CI 84.3–90.6 %) in the ESD series and 98.7 % (95 % CI 97.4–99.3 %) in the TEM series ($P < 0.001$, Fig. 2). Heterogeneity was greater in the ESD series ($I^2 = 60.1$ %) than in the TEM series ($I^2 = 46.4$ %).

The cumulative meta-analysis of all 18 studies showed a progressive increase from 81.4 to 95.1 % in the proportion of patients undergoing en bloc resection. The same proportion was quite constant (94.3–95.8 %), with no study strongly affecting the results in the influential, leave-one-out meta-analysis.

The R0 resection rate was available for 9 ESD and 8 TEM series. The pooled estimate of the proportion of patients was 74.6 % (95 % CI 70.4–78.4 %) in the ESD series and 88.5 % (95 % CI 85.9–90.6 %) in the TEM series ($P < 0.001$, Fig. 3). Heterogeneity was lower in the ESD series ($I^2 = 52.9$ %) than in the TEM series ($I^2 = 69.1$ %). The cumulative meta-analysis of all 17 studies showed a progressive increase from 62.9 to 82.7 % in the proportion of patients undergoing R0 resection. Again, the same proportion was quite constant (81.4–83.7 %) in the influential meta-analysis.

Perioperative complications

Data regarding perioperative complications were retrieved for all 11 ESD series and 8 of the TEM series. Altogether,

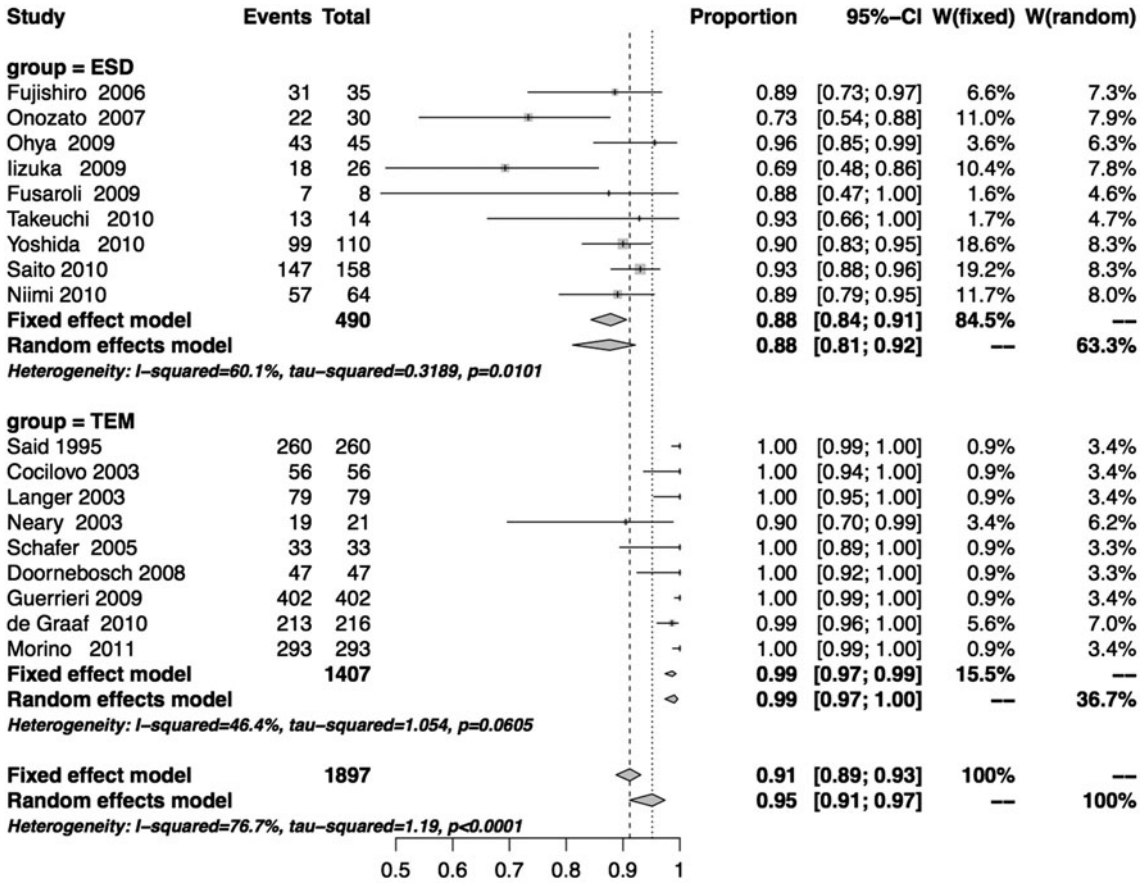

Fig. 2 En bloc resection rates for ESD and TEM, showing a statistically significant advantage of TEM ($P < 0.001$)

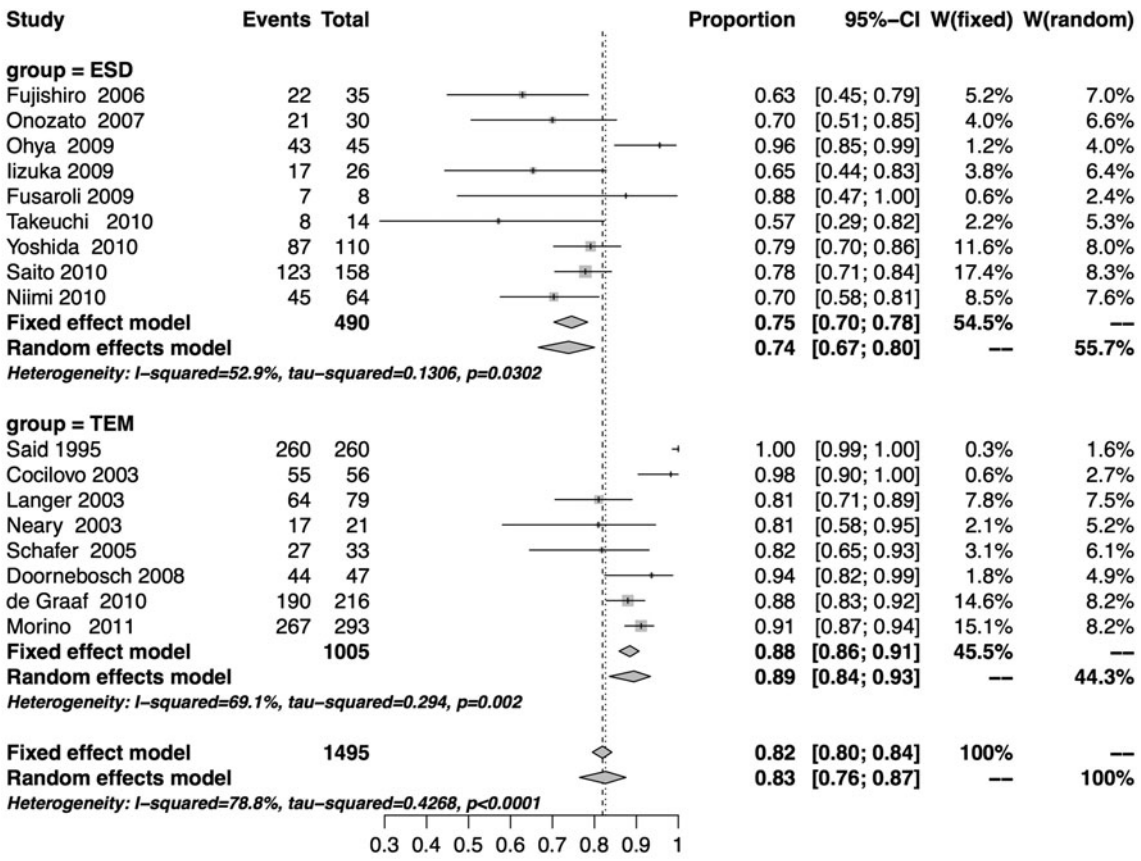

Fig. 3 R0 resection rates for ESD and TEM, showing a statistically significant advantage of TEM ($P < 0.001$)

1,887 patients (536 ESD and 1,351 TEM patients) were included in the analysis of complications. The complications after ESD were rectal bleeding ($n = 19$) and perforation ($n = 20$). The complications after TEM were suture leakage ($n = 43$), rectal bleeding ($n = 30$), fistulas ($n = 7$), urinary infection or retention ($n = 6$), and others ($n = 11$).

The proportion of patients with complications was 8.0 % (95 % CI 5.4–11.8 %) after ESD versus 8.4 % (95 % CI 5.2–13.4 %) after TEM (P = 0.874, Fig. 4). Heterogeneity was low in the ESD series ($I^2 = 25.0$ %) but extreme by comparison in the TEM series ($I^2 = 80.5$ %). A cumulative meta-analysis of all 19 studies showed a progressive increase from 4.2 to 8.6 % in the proportion of patients with complications. This proportion ranged from 7.1 to 8.7 %, without any single-trial effect, in the influential meta-analysis.

The pooled proportion of patients with perioperative events requiring additional abdominal surgery for complication control was 1.3 % (95 % CI 0.5–3.3 %) in the ESD series and 1.6 % (95 % CI 1.0–2.6 %) in the TEM series ($P = 0.665$, Fig. 5). Heterogeneity was absent in the ESD series ($I^2 = 0.0$ %) and low in the TEM series ($I^2 = 14.4$ %). A cumulative meta-analysis showed that 1.1–2.1 % of the patients required additional abdominal surgery. The influential meta-analysis showed a range of 1.3–1.7 %.

Histology

Only nine ESD and eight TEM series provided histology data. In all, 1,929 patients (488 ESD and 1,441 TEM patients) were included in the analyses of histology. Final pathology demonstrated an adenoma in 156 ESD patients (31.9 %) and 1,278 TEM patients (89.1 %), pTis or pT1sm1 cancers in 279 ESD patients (57.1 %) and 79 TEM patients (5.5 %), and invasive adenocarcinoma (pT1sm2 or more) in 45 ESD patients (9.2 %) and 73 TEM patients (5.1 %). Eight patients in the ESD group and four in the TEM group had another diagnosis.

The pooled estimate of the proportion of patients with invasive adenocarcinoma was 9.5 % (95 % CI 5.7–15.5 %) in the ESD series and 3.9 % (95 % CI 1.5–9.7 %) in the TEM series ($P = 0.095$). Heterogeneity was moderate in the ESD series ($I^2 = 50.7$ %) but extreme in the TEM series ($I^2 = 88.2$ %). The cumulative meta-analysis showed that 6.7–11.5 % of the patients required additional abdominal surgery. The influential meta-analysis showed a range of 5.0–7.8 %.

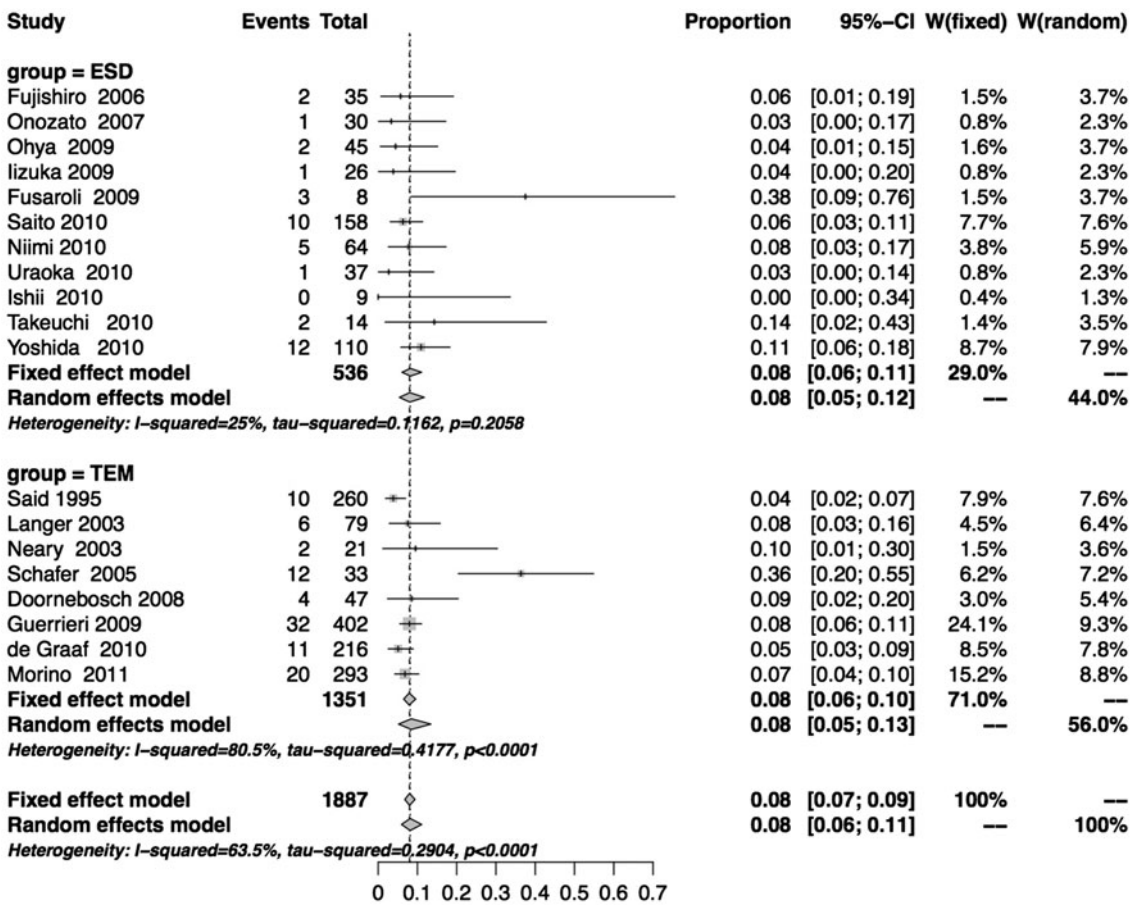

Fig. 4 Perioperative complication rates after ESD and TEM, showing substantial equivalence between the two groups ($P = 0.874$)

Recurrences and oncologic criteria

Only seven ESD series and nine TEM series provided recurrence data. All the ESD series reported a follow-up period of 6–12 months, whereas the TEM series reported an average follow-up period of 58.9 months (range, 1–204 months). In all, 1,811 patients (404 ESD and 1407 TEM patients) were included in the analyses of recurrences. The pooled estimate of the proportion of patients with adenoma recurrence was 2.6 % (95 % CI 1.3–5.2 %) in the ESD series and 5.2 % (95 % CI 4.0–6.9 %) in the TEM series ($P = 0.068$).

Heterogeneity was absent in the ESD series ($I^2 = 0.0$ %) and low in the TEM series ($I^2 = 21.5$ %). The pooled proportion of patients with perioperative events requiring additional abdominal surgery for oncologic indications or recurrence was 8.4 % (95 % CI 4.9–13.9 %) in the ESD series and 2.9 % (95 % CI 1.5–5.4 %) in the TEM series ($P = 0.011$). Heterogeneity was moderate in the ESD series ($I^2 = 40.2$ %) and greater in the TEM series ($I^2 = 63.3$ %).

Need for abdominal surgery

Data regarding the overall need for abdominal surgery, defined as any type of surgery performed through an abdominal access, were retrieved for eight ESD and nine TEM series. This included treatment of complications, recurrence, or major surgery for oncologic curative resection, as reported earlier. In all, 1,862 patients (455 ESD and 1407 TEM patients) were included in the analysis. The pooled estimate of the proportion of patients requiring abdominal surgery was 8.4 % (95 % CI 4.9–13.9 %) in the ESD series and 1.8 % (95 % CI 0.8–3.7 %) in the TEM series ($P < 0.001$, Fig. 6). Heterogeneity was moderate in both the ESD ($I^2 = 40.2$ %) and TEM ($I^2 = 48.1$ %) series.

Discussion

One of the most important risk factors for recurrence of rectal lesions is an R1 resection [2, 31, 32], which is

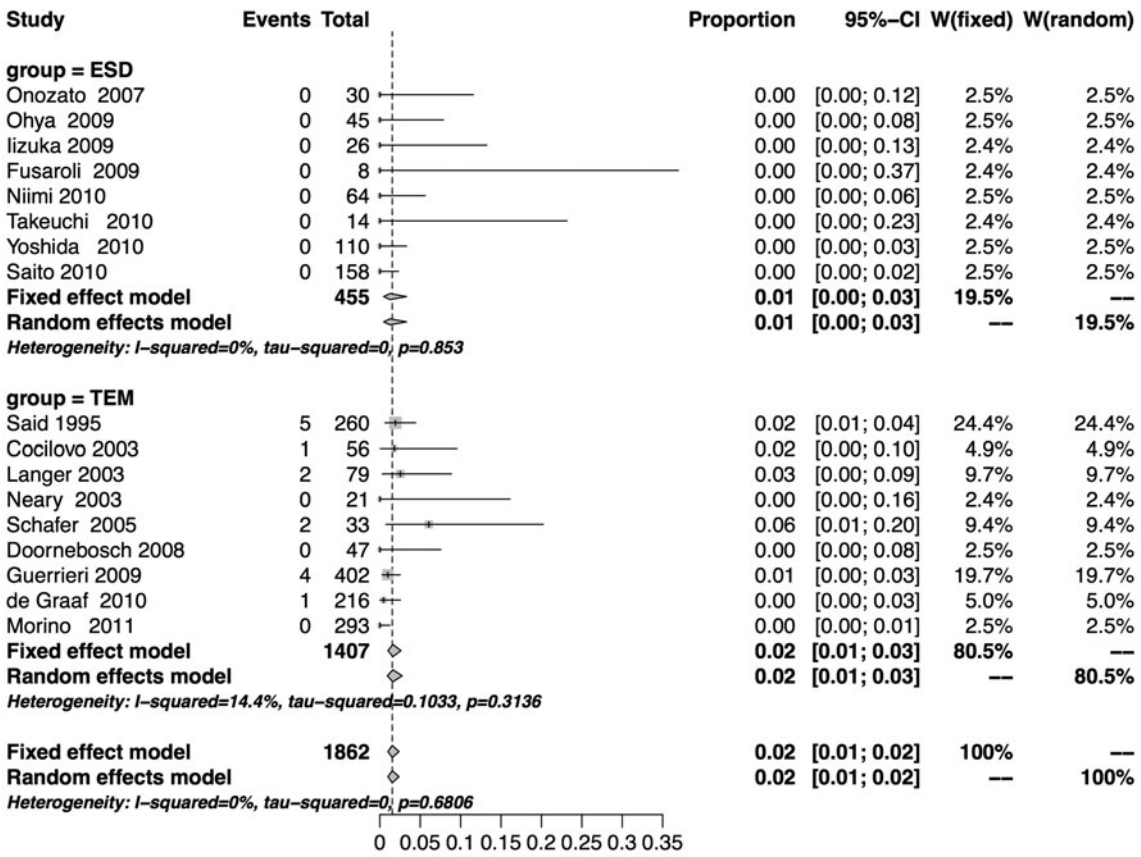

Fig. 5 Need for additional abdominal surgery for control of complications after ESD and TEM, showing a substantial equivalence between the two groups ($P = 0.665$)

obviously less probable when an en bloc resection is attempted. A recent systematic review by Barendse et al. [33] reported a recurrence rate of 11.2 % at 3 months after piecemeal EMR for colorectal lesions, which dropped to 1.5 % at 3 months after further endoscopic treatment. The authors claimed that this demonstrated the equivalence of EMR and TEM. However, the analysis contained a number of flaws. The two major flaws were that (1) all but one endoscopic series included only benign lesions, which suggested an evident selection of cases based on postoperative histology, and that (2) most of the TEM series included cases managed by a partial wall excision rather than a full-thickness technique, as suggested by most expert authors [29].

Due to the high rate of preoperatively misdiagnosed malignancies, piecemeal resection, as obtained by EMR, should not be performed when valid alternatives are available. Currently, surgeons performing endoscopic resection of a noninvasive rectal lesion should aim to use an ESD technique. Although rectal lesions currently are diagnosed earlier than in the past and can be treated with a variety of different techniques, we found no randomized or quasi-randomized study comparing ESD with TEM. Furthermore, although a meta-analysis of only randomized controlled trials would be ideal, case series data are the only evidence available to date.

The major limitation in the meta-analysis of the aforementioned data was the potential confounding by a systematic difference in patient characteristics between the two groups. In fact, although patients eligible for ESD will necessarily be assessed as having a superficial lesion, TEM often is performed also for those with an invasive lesion and almost always as a full-thickness excision. For this reason, we defined strict inclusion criteria that required a rectal lesion larger than 2 cm in diameter preoperatively assessed as a superficial neoplasm. By defining strict inclusion criteria, we excluded all TEM series that included preoperatively assessed malignant lesions because they were most probably biased by an extension of the inclusion criteria. The size limit requiring that lesions be larger than 2 cm was set according to the Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines [34], which aims to achieve en bloc resection with no fragmentation.

With these restrictions in selection, heterogeneity of the results was kept within a reasonable frame, although some of the study samples included in this analysis were relatively small. We also performed additional analyses to adjust for these potential confounders, which indicated that

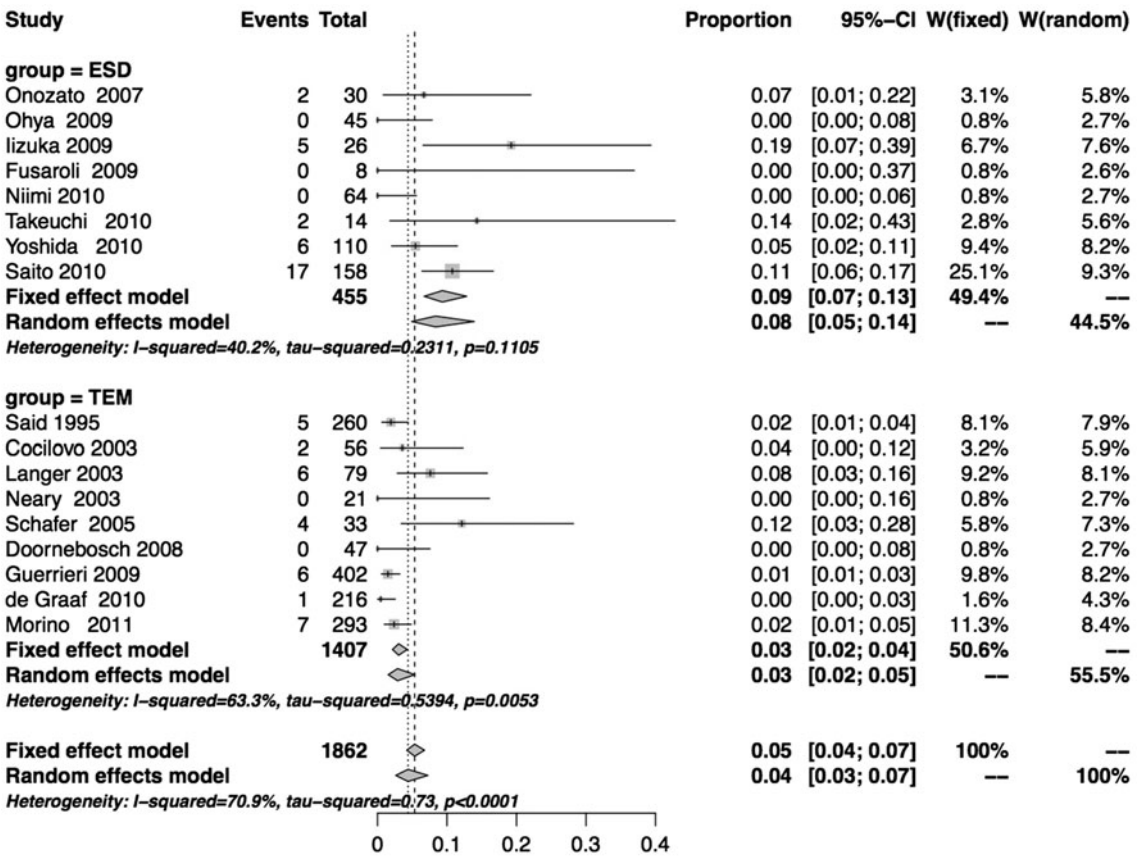

Fig. 6 Proportions of patients requiring abdominal surgery in the ESD and TEM series, showing a statistically significant lower incidence after TEM ($P < 0.001$)

their impact was null. By restricting the analysis to rectal lesions, we sought to limit any biases related to anatomic situations, which can influence the handling of lesions due to endoscope maneuverability restricted proximally to the rectum. As a consequence, the sensitivity analyses showed that no study had an influential effect on relative risk in the whole time frame.

A previous study comparing ESD with transanal excision (TAE) showed an advantage of ESD with respect to higher achievement of R0 en bloc resections [35]. Nonetheless, it is known that TEM is superior to TAE for the same reason, resulting in a significantly higher recurrence-free survival [36].

The TEM procedure remains the gold standard surgical treatment for rectal local excision. The pooled results of the current systematic review indicate that ESD for nonpedunculated superficial lesions of the rectum larger than 2 cm in diameter appears to be less effective than TEM, with an en bloc resection achieved for 88 % of patients compared with 99 % for TEM. Even more significantly, an R0 resection was achieved for 74 % of patients using ESD compared with 89 % using TEM. This difference was statistically significant. The apparently lower risk of recurrence shown in the ESD group was in fact not statistically significant, and in any case probably was due to the shorter follow-up period reported for the ESD series.

The ESD procedure is technically demanding with the currently available equipment and requires a significantly longer time to be completed. Yet the perioperative complication rate compared favorably with that of the TEM series, and the rate of abdominal surgery controlling complications was negligible.

Postoperative histology assessment demonstrated a much higher incidence of adenocarcinoma in the ESD series, which was attributable to a different way of classifying intramucosal lesions [37]. The rates of unpredicted invasive cancers treated in the two groups were comparable, but this required further surgery for oncologic reasons about four times more often in the ESD group due to the higher incidence of R1 resections than in the TEM group. In fact, a positive vertical margin after endoscopic resection is considered to be an indication for intestinal resection with lymph node dissection [34].

The high rate of further surgery for oncologic reasons after ESD also may explain the reduced risk of recurrence in this group. Although this could not be assessed through

the analysis of the selected papers, the reduced incidence of abdominal surgery after TEM might be due to the fact that patients with a cancer extended to the submucosal layer who received an R0 full-thickness resection often refused to undergo intestinal resection with lymph node dissection due to the limited risk of metastasis.

An indisputable advantage of ESD for rectal lesions is that it does not entail the need for general anesthesia or a prolonged hospital stay, as usually is the case after full-thickness TEM resection, although this more often is a trend or based on a difference in the practice of surgeons and endoscopists. On the other hand, TEM supporters could argue that preoperative assessment of benign or noninvasive lesions still is suboptimal, so that even in this analysis, a consistent number of cases actually resulted in malignancy.

The intraoperative finding of deep wall invasion misdiagnosed preoperatively can significantly influence oncologic outcome. Moreover, the risk for infiltration of the vertical margin is the only risk factor for recurrence and the reason why EMR should be avoided in such circumstances [34]. Of extreme interest would have been the influence on anal continence and rectal function, sexual and urinary dysfunction, and quality of life, but the lack of sufficient data on these issues precluded further analyses.

Based on the evidence of the current review and analysis, we can conclude that TEM achieves a higher rate of en bloc and R0 excision. As a consequence, full-thickness rectal wall excision by TEM significantly reduces the need for further abdominal treatment. How these results will ultimately translate into common daily clinical practice remains unclear. No randomized head-to-head comparisons between TEM and ESD have been performed to date. Our review clearly highlights the need for a large randomized study to obtain unbiased results on the effectiveness and safety of these two strategies for patients with large rectal lesions preoperatively assessed as adenomas or noninvasive neoplasms.

Disclosures Alberto Arezzo, Roberto Passera, Yutaka Saito, Taku Sakamoto, Nozomu Kobayashi, Naoto Sakamoto, Naohisa Yoshida, Yuji Naito, Mitsuhiro Fujishiro, Keiko Niimi, Tomohiko Ohya, Ken Ohata, Shinichi Okamura, Shinei Iizuka, Yoji Takeuchi, Noriya Uedo, Pietro Fusaroli, Marco Augusto Bonino, Mauro Verra, and Mario Morino have no conflicts of interest or financial ties to disclose.

References

1. Hermanek P, Gall FP (1986) Early (microinvasive) colorectal carcinoma: pathology, diagnosis, surgical treatment. Int J Colorectal Dis 1:79–84
2. Allaix ME, Arezzo A, Cassoni P et al (2012) Recurrence after transanal endoscopic microsurgery for large rectal adenomas. Surg Endosc 26:2594–2600
3. Ohkuwa M, Hosokawa K, Boku N et al (2001) New endoscopic treatment for intramucosal gastric tumors using an insulated-tip diathermic knife. Endoscopy 33:221–226
4. Tamegai Y, Saito Y, Masaki N et al (2007) Endoscopic submucosal dissection: a safe technique for colorectal tumors. Endoscopy 39:418–422
5. Higgins JPT, Green S (2010) Cochrane handbook for systematic reviews of interventions version 5.0.2 [updated September 2009]. The cochrane collaboration 2009. John Wiley & Sons, Ltd, Chichester
6. Moher D, Liberati A, Tetzlaff J et al (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 62:1006–1012
7. Buess G, Kipfmüller K, Hack D et al (1988) Technique of transanal endoscopic microsurgery. Surg Endosc 2:71–75
8. Kudo S, Rubio CA, Teixeira CR et al (2001) Pit pattern in colorectal neoplasia: endoscopic magnifying view. Endoscopy 33:367–373
9. Hozo SP, Djulbegovic B, Hozo I (2005) Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol 5:13–22
10. http://www.R-project.org. Accessed 1 Nov 2012
11. Fujishiro M, Yahagi N, Nakamura M et al (2006) Endoscopic submucosal dissection for rectal epithelial neoplasia. Endoscopy 38:493–497
12. Onozato Y, Kakizaki S, Ishihara H et al (2007) Endoscopic submucosal dissection for rectal tumors. Endoscopy 39:423–427
13. Ohya T, Ohata K, Sumiyama K et al (2009) Balloon overtube-guided colorectal endoscopic submucosal dissection. World J Gastroenterol 15:6086–6090
14. Iizuka H, Okamura S, Onozato Y et al (2009) Endoscopic submucosal dissection for colorectal tumors. Gastroenterol Clin Biol 33:1004–1011
15. Uraoka T, Ishikawa S, Kato J et al (2010) Advantages of using thin endoscope-assisted endoscopic submucosal dissection technique for large colorectal tumors. Dig Endosc 22:186–191
16. Ishii N, Itoh T, Horiki N et al (2010) Endoscopic submucosal dissection with a combination of small-caliber-tip transparent hood and flex knife for large superficial colorectal neoplasias including ileocecal lesions. Surg Endosc 24:1941–1947
17. Takeuchi Y, Uedo N, Ishihara R et al (2010) Efficacy of an endoknife with a water-jet function (Flushknife) for endoscopic submucosal dissection of superficial colorectal neoplasms. Am J Gastroenterol 105:314–322
18. Yoshida N, Naito Y, Kugai M et al (2010) Efficient hemostatic method for endoscopic submucosal dissection of colorectal tumors. World J Gastroenterol 16:4180–4186
19. Saito Y, Uraoka T, Yamaguchi Y et al (2010) A prospective, multicenter study of 1,111 colorectal endoscopic submucosal dissections (with video). Gastrointest Endosc 72:1217–1225
20. Fusaroli P, Grillo A, Zanarini S et al (2009) Usefulness of a second endoscopic arm to improve therapeutic endoscopy in the lower gastrointestinal tract: preliminary experience: a case series. Endoscopy 41:997–1000
21. Niimi K, Fujishiro M, Kodashima S et al (2010) Long-term outcomes of endoscopic submucosal dissection for colorectal epithelial neoplasms. Endoscopy 42:723–729
22. Said S, Stippel D (1996) 10 years experiences with transanal endoscopic microsurgery. Histopathologic and clinical analysis. Chirurg 67:139–144
23. Cocilovo C, Smith LE, Stahl T et al (2003) Transanal endoscopic excision of rectal adenomas. Surg Endosc 17:1461–1463
24. Langer C, Liersch T, Suss M et al (2003) Surgical cure for early rectal carcinoma and large adenoma: transanal endoscopic microsurgery (using ultrasound or electrosurgery) compared to

conventional local and radical resection. Int J Colorectal Dis 18:222–229
25. Neary P, Makin GB, White TJ et al (2003) Transanal endoscopic microsurgery: a viable operative alternative in selected patients with rectal lesions. Ann Surg Oncol 10:1106–1111
26. Schafer H, Baldus SE, Holscher AH (2006) Giant adenomas of the rectum: complete resection by transanal endoscopic microsurgery (TEM). Int J Colorectal Dis 21:533–537
27. Ganai S, Kanumuri P, Rao RS et al (2006) Local recurrence after transanal endoscopic microsurgery for rectal polyps and early cancers. Ann Surg Oncol 13:547–556
28. Doornebosch PG, Gosselink MP, Neijenhuis PA et al (2008) Impact of transanal endoscopic microsurgery on functional outcome and quality of life. Int J Colorectal Dis 23:709–713
29. Guerrieri M, Baldarelli M, de Sanctis A et al (2010) Treatment of rectal adenomas by transanal endoscopic microsurgery: 15 years' experience. Surg Endosc 24:445–449
30. de Graaf EJ, Burger JW, van Ijsseldijk AL et al (2011) Transanal endoscopic microsurgery is superior to transanal excision of rectal adenomas. Colorectal Dis 13:762–767
31. Morino M, Allaix ME, Caldart M et al (2011) Risk factors for recurrence after transanal endoscopic microsurgery for rectal malignant neoplasm. Surg Endosc 25:3683–3690
32. Allaix ME, Arezzo A, Caldart M et al (2009) Transanal endoscopic microsurgery for rectal neoplasms: experience of 300 consecutive cases. Dis Colon Rectum 52:1831–1836
33. Barendse RM, van den Broek FJ, Dekker E et al (2011) Systematic review of endoscopic mucosal resection versus transanal endoscopic microsurgery for large rectal adenomas. Endoscopy 43:941–949
34. Watanabe T, Itabashi M, Shimada Y et al (2012) Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2010 for the treatment of colorectal cancer. Int J Clin Oncol 17:1–29
35. Kiriyama S, Saito Y, Matsuda T et al (2011) Comparing endoscopic submucosal dissection with transanal resection for non-invasive rectal tumor: a retrospective study. J Gastroenterol Hepatol 26:1028–1033
36. Moore JS, Cataldo PA, Osler T, Hyman NH (2008) Transanal endoscopic microsurgery is more effective than traditional transanal excision for resection of rectal masses. Dis Colon Rectum 51:1026–1030
37. Schlemper RJ, Itabashi M, Kato Y et al (1998) Differences in the diagnostic criteria used by Japanese and Western pathologists to diagnose colorectal carcinoma. Cancer 82:60–69

Surg Endosc
DOI 10.1007/s00464-016-5362-3

Colonic stenting as a bridge to surgery versus emergency surgery for malignant colonic obstruction: results of a multicentre randomised controlled trial (ESCO trial)

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Received: 24 July 2016 / Accepted: 13 November 2016

Abstract
Background The aim of colonic stenting with self-expandable metallic stents in neoplastic colon obstruction is to avoid emergency surgery and thus potentially reduce morbidity, mortality, and need for a stoma. Concern has been raised, however, about the effect of colonic stenting on short-term complications and long-term survival. We compared morbidity rates after colonic stenting as a bridge to surgery (SBTS) versus emergency surgery (ES) in the management of left-sided malignant large-bowel obstruction.
Methods This multicentre randomised controlled trial was designed with the endorsement of the European Association for Endoscopic Surgery. The study population was consecutive patients with acute, symptomatic malignant left-sided large-bowel obstruction localised between the splenic flexure and 15 cm from the anal margin. The primary outcome was overall morbidity within 60 days after surgery.
Results Between March 2008 and November 2015, 144 patients were randomly assigned to undergo either SBTS or ES; 29/144 (13.9%) were excluded post-randomisation mainly because of wrong diagnosis at computed tomography examination. The remaining 115 patients (SBTS $n = 56$, ES $n = 59$) were deemed eligible for analysis. The complications rate within 60 days was 51.8% in the SBTS group and 57.6% in the ES group ($p = 0.529$). Although long-term follow-up is still ongoing, no statistically significant difference in 3-year overall survival ($p = 0.998$) and progression-free survival rates between the groups has been observed ($p = 0.893$). Eleven patients in the SBTS group and 23 in the ES group received a stoma ($p = 0.031$), with a reversal rate of 30% so far.
Conclusions Our findings indicate that the two treatment strategies are equivalent. No difference in oncologic outcome was found at a median follow-up of 36 months. The significantly lower stoma rate noted in the SBTS group argues in favour of the SBTS procedure when performed in expert hands.

Keywords Large bowel obstruction · Endoscopic stenting · Bridge to surgery · Emergency colorectal surgery · Randomized controlled trial

Elective colonic surgery is considered a safe procedure, with a low risk of post-operative anastomosis leakage, whereas emergency colonic surgery is associated with consistent morbidity and mortality rates [1]. Emergency surgery patients are generally older and often present with multiple comorbidities and bowel distension [2]. An alternative to emergency surgery is stenting with self-expandable metallic stents (SEMSs). Clinical and technical successes of stenting with SEMS in various regions of the gastrointestinal tract, including the oesophagus, duodenum, and biliary tract, have been reported over the last 30 years. Endoscopic stent placement was extended to the treatment

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Published online: 06 December 2016

of neoplastic colonic obstruction initially with palliative intent [3], then later as preoperative decompression and as palliative final treatment with good preliminary results [4].

The aim of stenting with SEMS in an obstructed colon is to transform an emergency surgical case into an elective surgery case and restore bowel transit, thus reducing morbidity, mortality, and the need for an enterostomy. Several randomised controlled trials (RCTs) and case-matched studies have reported controversial results and expressed concern regarding the effect of colonic stenting on short-term complications long-term survival in patients with potentially curable disease, due to the potential risk of local advancement of the cancer and metastatic spread [5, 6]. With this study, we compared morbidity rates after colonic stenting as a bridge to surgery and after emergency surgery to evaluate the efficacy and safety of the two strategies in the management of malignant, left-sided large-bowel obstruction.

Methods

This multicentre RCT was designed with the endorsement of the European Association for Endoscopic Surgery (EAES). The project was approved by the Local Ethics Committee of the Città Della Salute e Della Scienza Di Torino, University of Torino, Italy, which served as the principle study centre. The project was registered with ClinicalTrials.gov, US International Clinical Trials Databank (US National Institutes of Health), ID-code NCT00591695, on behalf of the EAES. The study design conformed with CONSORT criteria.

Study population

The main inclusion criterion was acute, symptomatic malignant left-sided large-bowel obstruction localised between the splenic flexure and 15 cm from the anal margin, as diagnosed by computed tomography (CT) examination in the emergency room. The main clinical complaint was failure to pass gas and faeces. Exclusion criteria were bowel perforation as diagnosed by clinical exploration and complementary studies, associated conditions contraindicating general anaesthesia and/or haemodynamic instability, impossibility to obtain valid informed consent or refusal by the patient, distant metastases as diagnosed by CT scan at the time of diagnosis.

Patient recruitment

Consecutive eligible patients were recruited at the emergency room of the participating centres. Patients fulfilling the above-mentioned criteria were informed about the aim of the study by a clinician involved in the study. Patients granting informed consent were randomly assigned to one of the two study arms and treated according to the study protocol. Participating centres had to demonstrate that more than 25 SEMS placement procedures had been performed with a documented complications rate not higher than that reported in the literature.

Randomisation

Patient data were entered into a centralised web-based database and blind randomisation was done by means of an unchangeable number-generating software programme. Randomisation was stratified per single centre and according to tumour stage (T4 vs. others). Patients were randomly assigned to receive either stent bridge to surgery (SBTS) followed by elective surgery (if successful) or emergency surgery (ES). Treatments were planned within 24 h after diagnosis.

Operative technique

In the SBTS treatment arm, SEMS placement was performed using a colonoscope with a 4.2-mm operative channel. A hydrophilic guide contained in a five Fr catheter was advanced across the neoplastic stenosis under radiographic control. The catheter was inserted through the stenosis and water-soluble contrast liquid injected above the stenosis to evaluate the length of the stenosis under fluoroscopic vision. A super stiff guide wire was left in place while the five Fr catheter was retracted. Stents were positioned so as to exceed 1–2 cm from each side of the stenosis. No tumour or stent dilatation was performed. Technical success was defined as correct stent placement under radiographic and endoscopic vision. Clinical success was defined as resolution of occlusive symptoms by gas and faeces passage. Emergency surgery was indicated in case of technical or clinical failure. If symptom relief was achieved with stenting, elective surgery was scheduled depending on the patient's clinical conditions and included laparoscopic or laparotomic bowel resection, with or without creation of a protective stoma, according to surgeons' preferences and intra-operative findings.

In the ES treatment arm, surgeons could decide between simple enterostomy and bowel resection based on their experience, the patient's clinical condition, and intra-operative findings. Bowel resection could be performed using Hartmann's procedure, on table irrigation, and primary anastomosis or subtotal colectomy.

Preoperative, intra-operative, and post-operative care, including adjuvant therapy protocols and follow-up, were

carried out in accordance with the standards of care at each centre and were the same for all patients at each centre.

Primary end point

Overall morbidity was defined as any surgery-related morbidity diagnosed within 60 days after surgery. Morbidity was defined as the occurrence of any complication directly or indirectly related to endoscopy and/or surgery. Complications were classified according to Dindo [7].

Secondary end points

Technical success and clinical success of SEMS placement were defined as correct stent placement under both radioscopic and endoscopic inspection and as resolution of occlusive symptoms by passage of gas and faeces, respectively. Operative time was defined as the length of time in minutes between skin incision and end of skin closure. Hospital stay was defined as the length of hospital stay in days between admission to and discharge from hospital.

Post-operative complications during hospital stay were defined as any local or systemic complications observed during hospital stay. Complications at 60 days were defined as any local or systemic complications still observed at 60 days after initial treatment.

Oncologic outcome *was* defined as the comparison of the log-rank overall and progressive disease curves of the two groups for a minimum of 3 years unless censored. Quality of life was measured using the 36-item Short Form Health Survey (SF-36) at 60 days after surgery.

Sample size and power calculation

Assuming a baseline overall morbidity within 60 days of 15% after SBTS and of 35% after ES (average morbidity based on the literature), a total of 144 patients was needed to prove superiority of SBTS over ES, with a β-error of 0.2 and an α-error of 0.05.

Data analysis

Intra- and post-operative data were entered by the recruiting clinician in a web-based database at any time during the study. Patients' personal data were protected against unauthorised or accidental access. All analyses were carried out primarily on an intention-to-treat basis.

Data monitoring

An expert in colorectal surgery and endoscopy was designated as data monitor. He had access to the data during the entire course of the study and could recommend cessation of the trial if one arm was providing manifestly inferior results.

Statistical analysis

Categorical variables are described as frequencies and percentages, while median and interquartile ranges (IQR) (in brackets) report continuous variables. Fisher's exact test was performed to evaluate the association between any categorical variable and the treatment arm (SBTS/ES), while the Mann–Whitney test was used for continuous variables. The primary end points for survival analyses were overall survival (OS) and progression-free survival (PFS). OS was defined as the time from accrual to death from any cause, and PFS as the time from accrual to progression/relapse/death from any cause, whichever came first. In both cases, patients still alive were censored at the date of last contact. OS and PFS curves were estimated by the Kaplan–Meier method and compared using the log-rank test. All reported p values were obtained using a two-sided exact method at the conventional 5% significance level. Data were analysed as of June 2016 by R 3.2.3 (R Foundation for Statistical Computing, Vienna-A, http://www.R-project.org).

Results

Upon receipt of approval from the ethics committee, enrolment was started on 1 March 2008 and closed on 16 November 2015. Five centres were involved in the study (Table 1). Of the 144 initially randomised patients, 29 were excluded post-randomisation: 20 (13.9%) because of wrong diagnosis at CT, one patient because no endoscopist was free to attend, and eight patients withdrew consent (Table 2). Table 3 presents the distribution of the remaining 115 patients at the various centres; the patients' characteristics are given in Table 4. Figure 1 illustrates the patients' flow chart.

The occlusion site was the splenic flexure in 18 patients (5 in the SBTS and 13 in the ES group), the descending colon in 77 (43 in the SBTS and 34 in the ES group), and the sigmoid colon in 20 (8 in the SBTS and 12 in the ES group) ($p = 0.055$). Stents of four different diameters were used: 20 mm in four cases, 22 mm in 21, 24 mm in 2, 25 mm in 15, and 30 mm in 5; stent diameter was not reported in seven cases. Technical success was reported in 49 of the 56 stented patients. Eight cases of stent-related complications occurred: perforation in 5, bleeding in 1, relevant pain 1, and pulmonary infection due to aspiration in 1. All five cases of perforation occurred at the tumour site (the descending colon in three and the sigmoid tract in

Table 1 Distribution of patients initially randomised by study centre

Study centre	Patients ($N = 144$)
University of Torino, Torino, Italy	53
ASO Santa Croce e Carle, Cuneo, Italy	40
Hospital de la Sta Creu i St Pau, Barcelona, Spain	32
Hospital General Universitario de Elche, Alicante, Spain	12
Humanitas Gradenigo Hospital, Torino, Italy	7

Table 2 Causes of dropout from the study

	SBTS group	ES group	Total no. (%)
Diverticulitis	5	6	11 (7.6)
Faecaloma	1	1	2 (1.4)
Colonic pseudo-obstruction	2	0	2 (1.4)
CDAD	1	0	1 (0.7)
Ischaemic colitis	1	0	1 (0.7)
Synchronous neoplasm	1	0	1 (0.7)
No stenosis at endoscopy	1	1	2 (1.4)
Endoscopist unavailable	1	0	1 (0.7)
Consent withdrawn	5	3	8 (5.6)
Overall total	18	11	

SBTS stenting as a bridge to surgery, *ES* emergency surgery, *CDAD Clostridium difficile* associated diarrhoea

Table 3 Distribution of patients by study centre

Hospital participating in the study	SBTS ($N = 56$)	ES ($N = 59$)
Dept. of Surgical Sciences, University of Torino, Italy	21	22
ASO Santa Croce e Carle, Cuneo, Italy	16	16
Hospital de la Sta Creu i St Pau, Barcelona, Spain	12	15
Hospital General Universitario de Elche, Alicante, Spain	5	5
Humanitas Gradenigo Hospital, Torino, Italy	2	1

SBTS stenting as a bridge to surgery, *ES* emergency surgery

Table 4 Clinical characteristics of patients allocated to treatment with stenting as a bridge to surgery (SBTS) or emergency surgery (ES)

	SBTS group ($N = 56$)	ES group ($N = 59$)	p value
Sex (M/F)	28/28	32/27	0.711
Mean age (years)	72 (range 43–90)	71 (range 44–94)	0.606
Age >70	29	30	0.920
BMI	24.8 (range 19.5–40.2)	24.5 (range 18–35)	0.608
ASA classification			0.775
ASA I	12	11	
ASA II	27	28	
ASA III	14	16	
ASA IV	3	4	

BMI body mass index (weight in kg divided by height in m squared)

two). Six patients required emergency surgery. Clinical success was achieved in 44 (78.6%) patients.

The median time between SEMS placement and elective surgery was 5 days (range 3–8). Table 5 presents the type of surgery performed in the two groups ($p < 0.001$). Eleven patients (22.2%) in the SBTS group and 23 (39%) in the ES group ($p = 0.031$) received a stoma, which consisted of an end colostomy of the left colon in all cases,

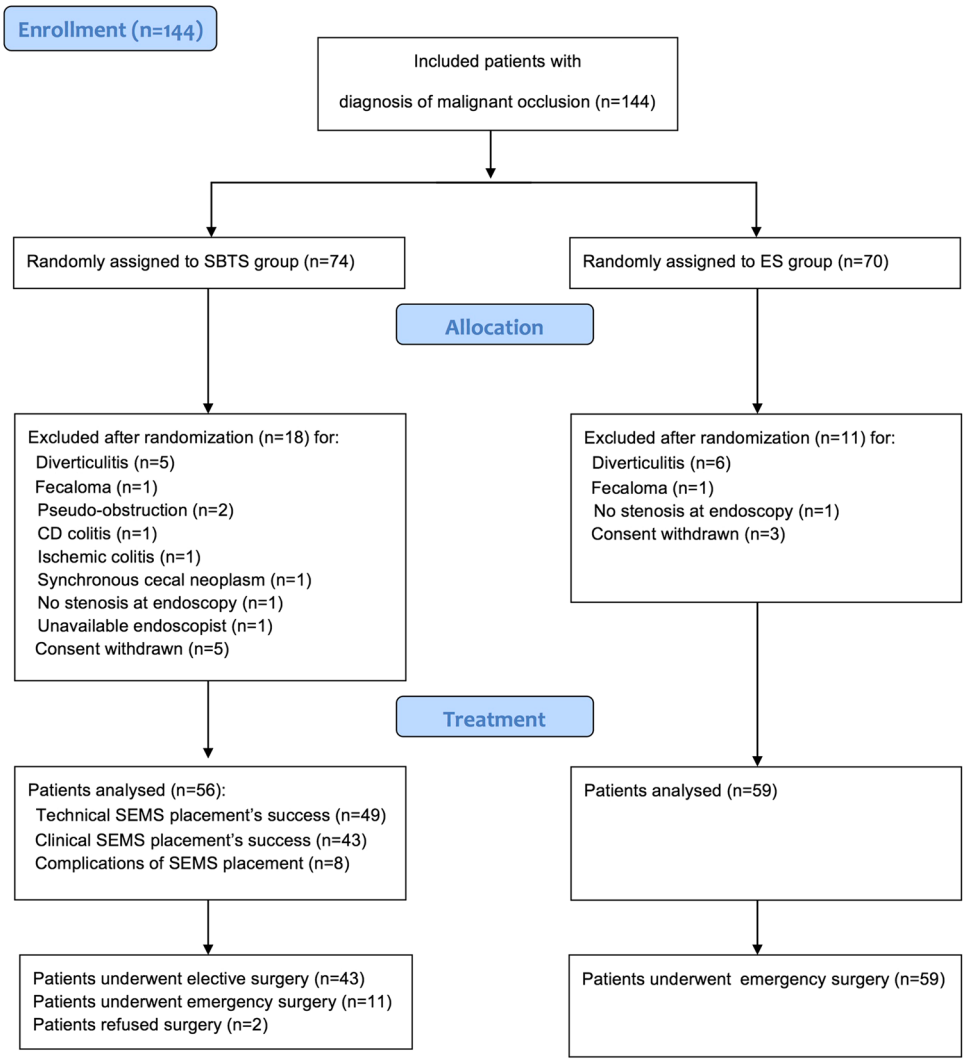

Fig. 1 CONSORT 2010 flow diagram

Table 5 Type, number, and percentage (%) of surgical procedures

Surgery	SBTS group ($N = 54$)	ES group ($N = 59$)	p value
Hartmann's procedure	11 (20.4)	20 (33.9)	
Subtotal colectomy	2 (3.6)	15 (25.4)	
Washout and anastomosis	1 (1.8)	10 (16.9)	
Colostomy	0	1 (1.7)	
Left colectomy	27 (50)	11 (18.6)	
Sigmoidectomy	11 (20.4)	2 (3.4)	
Anterior resection	2 (3.7)	0	
Overall total	54	59	<0.001

SBTS stenting as a bridge to surgery, *ED* emergency surgery

except one in which a lateral colostomy without bowel resection was performed due to peritoneal carcinomatosis. No association was observed between time to elective surgery after stenting and need for a stoma ($p = 0.845$).

The median operative time was 165 min in the SBTS group (range 120–200) and 180 min in the ES group (range 150–210) ($p = 0.098$). A laparoscopic approach was used in 23 (41.1%) stented patients, in 17 (30.3%) of which resection was completed laparoscopically and by conversion to open surgery in 6.

Post-operative complications during hospital stay were classified as local or systemic and were multiple in some

cases. Local complications developed in 9 (16.7%) patients in the SBTS group (anastomotic leakage in 3, intra-abdominal abscess in 1, ileus in 2, wound infection in 4, and wound haematoma in 1) and 12 (20.3%) in the ES group (anastomotic leakage in 2, ileus in 2, colostomy-related complication in 1, and wound infection in 7) ($p = 0.616$). Systemic complications developed in 14 (25.9%) patients in the SBTS group (pneumonia in 2, urinary complications in 3, acute pulmonary embolism in 1, sepsis in 4, anaemia in 2, heart failure in 2, and diarrhoea in 2) and in 21 (36.2%) in the ES group (pneumonia in 2, urinary complications in 5, multiorgan failure in 2, pulmonary thromboembolism in 1, sepsis in 3, anaemia in 3, heart failure in 3, diarrhoea in 5, hepatic failure in 1, respiratory failure in 1, and neurological complications in 2) ($p = 0.214$). One patient in the SBTS group died after stent placement due to perforation and 1 refused surgery after stent placement. One patient in the ES group received a colostomy without resection due to peritoneal carcinomatosis (Fig. 2).

Parenteral nutrition was administered in 18 (32.1%) patients in the SBTS and in 27 (45.8%) in the ES group ($p = 0.135$). Blood transfusion was given in 7 (12.5%) patients in the SBTS and in 11 (18.6%) in the ES group ($p = 0.365$). The median length of hospital stay was 15 days in the SBTS group (range 12–20) and 11 days in the ES group (range 8–15) ($p < 0.001$). The median length of hospital stay after surgery was 10 days in the SBTS (range 7–13) and 11 days in the ES group (range 8–15) ($p = 0.039$).

Definitive histology of the surgical specimen showed pT2 adenocarcinoma in two patients, pT3 in 37, and pT4 in 15 in the SBTS group, and pT2 adenocarcinoma in one patient, pT3 in 36 patients, and pT4 in 21 in the ES group ($p = 0.547$). Infiltrated resection margins were noted in two patients in the ES group. Tumour grade was G1 in 14 patients, G2 in 35, and G3 in 5 in the SBTS group, and G1 in 12 patients, G2 in 34, and G3 in 12 in the ES group ($p = 0.233$). Lymph node status was pN0 in 27 patients, pN1 in 19, and pN2 8 in the SBTS group, and pN0 in 27 patients, pN1 in 20, and pN2 in 11 in the ES group ($p = 0.837$). The number of harvested lymph nodes was <12 in 9 (16.7%) patients in the SBTS group and 15 (25.9%) in the ES group ($p = 0.236$). The median number of lymph nodes harvested was 18 in the SBTS group (range 12–21) and 15 in the ES group (range 11–19) ($p = 0.098$). Liver metastases were discovered during surgery in four patients from each group ($p = 0.897$).

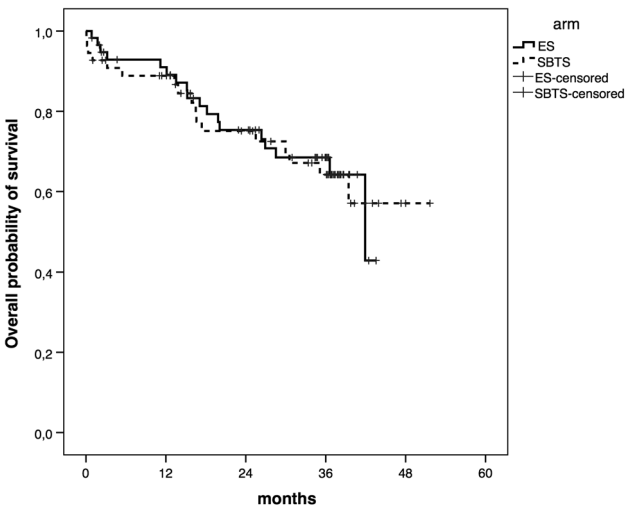

Fig. 2 Kaplan–Meier overall probability of survival

Local complications at 60 days after surgery were recorded in three patients in the SBTS group (wound infection in 1, parastomal hernia in 1, and ileus in 1) and in 2 in the ES group (wound infection in 1 and severe perianal dermatitis in 1) ($p = 0.605$), while systemic complications developed in five patients in the SBTS group (diarrhoea in 2, thrombocytopenia in 1, and constipation in 2) and in 2 in the ES group (diarrhoea in 1 and urinary tract infection in 1) ($p = 0.214$).

Post-surgical complications within 60 days after surgery were recorded in 29 patients (51.8%) in the SBTS group and in 34 (57.6%) in the ES group, demonstrating a substantial equivalence between the two groups in terms of morbidity ($p = 0.529$). Complications were classified according to Dindo [7] (Table 6). No substantial difference between the groups was observed ($p = 0.269$). Four patients in the SBTS group died (2 from septic shock, 1 from pneumonia, and 1 from disease progression) and 3 in the ES group (1 from septic shock, 1 from pneumonia, and 1 from disease progression) ($p = 0.943$).

At a median follow-up of 36 months (range 16–38), 17 relapses (30.3%) were observed in the SBTS group and 20 (33.9%) in the ES group ($p = 0.685$) (Table 7). Stoma reversal, which entailed reversal of a Hartmann's procedure in all cases, was performed in 2/11 patients (18.2%) in the SBTS group and in 8/23 (34.8%) in the ES group

Table 6 Number and percentage (%) of patients presenting with complications after colonic stenting as a bridge to surgery (SBTS) or emergency surgery (ES) according to the Dindo classification

Complication	SBTS group	ES group	*p* value
Grade I	10 (17.9)	11 (18.6)	
Grade II	8 (14.3)	12 (20.3)	
Grade IIIa	0	2 (3.4)	
Grade IIIb	7 (12.5)	3 (5.1)	
Grade IVa	0	3 (5.1)	
Grade IVb	0	0	
Grade V	4 (7.1)	3 (5.1)	
Overall total	29	34	0.269

Table 7 Number and percentage (%) of patients with disease recurrence

Recurrence	SBTS group	ES group	*p* value
Locoregional	6 (10.7)	7 (11.9)	
Liver	7 (12.5)	4 (6.8)	
Lung	2 (3.6)	1 (1.7)	
Laparotomy wound	0	1 (1.7)	
Pelvic	1 (1.8)	3 (5.1)	
Carcinomatosis	1 (1.8)	2 (3.4)	
Uterus	0	1 (1.7)	
Bladder	0	1 (1.7)	
Overall total	17	20	0.685

SBTS stenting as a bridge to surgery, *ES* emergency surgery

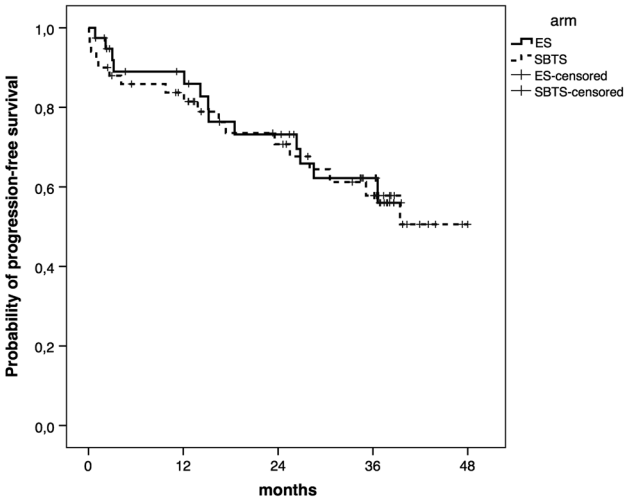

Fig. 3 Kaplan–Meier probability of progression-free survival

($p = 0.320$), for a total stoma reversal rate of 29.4% (10/34 patients). Eight patients have not had their stoma reversed so far due to progressive disease (2 in the SBTS and 6 in the ES group) and 16 patients due to poor clinical conditions (7 in the SBTS and 9 in the ES group). Adjuvant therapy was planned in 48 patients in the SBTS group and 55 in the ES group; however, treatment could not be initiated due to persisting complications in 16/48 (33.3%) in the SBTS group and 17/55 (30.9%) in the ES group ($p = 0.793$). At follow-up 1 year after surgery, 34 (60.7%) patients in the SBTS group and 41 (69.4%) in the ES group presented with post-operative complications ($p = 0.323$).

Analysis of the data from 79.2% of patients who completed the minimum follow-up of 3 years or censored showed that overall survival and progression-free survival in the two groups were comparable ($p = 0.998$ and $p = 0.893$, respectively) (Tables 2, 3).

Unfortunately, the data about quality of life measured with the SF-36 were insufficient for inferential analysis.

Discussion

Bowel obstruction is a medical and surgical emergency. A key hypothesis driving surgeons' interest in the use of SEMS placement in colonic obstruction is that it could convert an emergency surgery into an elective one, thus potentially reducing preoperative morbidity, restore bowel function, and avoid the need for a stoma, which is more often permanent rather than temporary and significantly diminishes the patient's quality of life. Our findings are shared by those reported by Van Hooft et al. [8] and showed a fairly similar morbidity rate within 60 days after surgery and mortality rate in both treatment groups (Fig. 3).

Extremely relevant in this context is the unexpectedly high rate of wrong diagnosis due to complicated diverticulitis in some cases and in others to a variety of clinical findings, which, if discovered intra-operatively, could severely burden clinical outcome. This is why it seemed questionable, whether stenting was indicated or not, if flexible colonoscopy should have been performed preoperatively in either all cases or none.

The sample size of our study was calculated based on the literature, essentially retrospective series, available at the time the protocol was conceived. We had initially calculated a 35 and a 15% overall complications rate after ES and SBTS, respectively. Contrary to our expectations, however, we observed rates of 57.6 and 51.8%, respectively, which are far higher than what we anticipated. This most probably stems from use of the Dindo classification, which defines complications as any sort of deviation from the normal post-operative course even without the need for pharmacological treatment or surgical, endoscopic or radiological interventions. These are classified as grade I complications and account for more than one-third of the complications reported in our study. A similar finding was observed by Van Hooft et al. [8] who also classified complications according to Dindo and found that grade I complications accounted for 40% of all post-operative complications.

Major concern has been raised regarding oncologic outcome after SBTS and the increased risk of disease spread, particularly of liver metastases. Sabbagh reported significantly lower overall survival rates in the SBTS group (25 vs. 62%, $p = 0.0003$), even among those without perforation or metastasis at diagnosis [6]. These findings contrast with the prospective RCTs published by Alcantara et al. [9] and Cheung [10], however. Furthermore, Sloothaak reported that, although stent placement was

associated with a higher risk of recurrence, the numbers were too small to draw a definitive conclusion from the long-term results of the Stent-In 2 trial. While subgroup analysis indeed showed a higher rate of recurrence among patients who experienced perforation during SEMS placement, we now know that one of the weaknesses of the study was the variation in operator experience with stenting in the participating centres, which could partly explain the high rate of perforations as compared with the published literature [11]. As a result, in order to minimise the risk of perforation, surgeons in the Netherlands must prove sufficient expertise before they can perform colonic stenting. The general consensus is that further larger trials are mandatory and that stent placement should be performed only in centres where experienced endoscopists are available [12–15].

The overall survival and progression-free survival curves for our series show comparable results between the two groups. This might be related to the fact that the majority of patients were treated at three centres with proven expertise in operative endoscopy, as shown by a 78.6% clinical success rate with SEMS placement, which is consistent with previous RCTs.

Moreover, Kim recently reported a higher number of stented patients with at least 12 lymph nodes harvested [16]. In our series, the number of patients who had at least 12 lymph nodes harvested at surgery was similar in the two groups; however, while we observed that the median number of harvested lymph nodes was significantly higher in the SBTS group, it is not clear whether this difference is relevant in terms of oncologic outcome. Until further data become available, no relation can be established between oncologic outcome and number of harvested lymph nodes.

It might be argued that a limitation of our study is that, while clinicians skilled in colonic stent placement were included, because the surgical procedure/technique was not standardised across all centres, our conclusions regarding stoma formation are based completely on "surgeon's preference". The options for performing bowel resection included Hartmann's procedure, on table irrigation, and primary anastomosis or subtotal colectomy, according to the protocol. We acknowledge that this led to sizeable variability in treatment; nevertheless, we felt that surgeons experienced in colorectal surgery would find standardisation stifling when on duty in the emergency room. Also, there is no clear evidence that one procedure may be better than another among those we included in the present study.

Unfortunately, we were unable to collect sufficient quality of life data. The need for stoma creation was significantly lower in the SBTS group and only about 30% of the patients have had their stoma reversed so far, which holds particular importance for patients' perception of quality of life. Moreover, a consistently higher incidence of subtotal colectomy was recorded in the ES group ($p = 0.001$), which further burdens the quality of life of patients, as documented by the SCOTIA study [17]. Given the fairly similar morbidity rates and substantially equivalent oncologic outcomes, SBTS in the management of left-sided malignant colonic obstruction seems a reasonable strategy that can be adjusted when subgroup analyses identify preferable indications.

The current guidelines of the European Society of Gastrointestinal Endoscopy (ESGE) [18] explicitly state that colonic SEMS placement as a bridge to elective surgery is not recommended as a standard treatment of symptomatic left-sided malignant colonic obstruction (strong recommendation, high-quality evidence). The authors of the guidelines mention that some advantages of SEMS as a bridge to surgery are supported by a recent meta-analysis [19] of RCTs. However, the observation of a higher oncologic risk associated with perforation prompted the authors to recommend a more cautious use of stents. The motivation for this recommendation seems to have derived from the findings of a single RCT [11], where it did not translate into a worse overall survival. Nevertheless, the authors concluded that the oncological risks of SEMS should be balanced against the operative risks of emergency surgery. As there is no reduction in post-operative mortality and stenting seems to impact on oncological safety, the use of SEMS as a bridge to elective surgery is not recommended as a standard treatment for potentially curable patients with left-sided malignant colonic obstruction, except in patients at high surgical risk. We believe that, in the light of our findings, the current guidelines should be reconsidered regarding the use of SEMS in an SBTS strategy, at least in high-volume centres.

A final point is that the time to restoration of bowel function varies from individual to individual and that delayed return of normal bowel activity can prolong hospital stay after SBTS. While this is definitely true, especially in settings where an early discharge policy after stenting is not practiced, it is also true that in-hospital stay calculated as the time between surgery and discharge was significantly shorter in the SBTS group. A future area of focus should be to optimise and standardise protocols for post-stent care, including in-hospital stay and the need for proper bowel preparation.

Conclusions

This is the largest multicentre randomised controlled study to date that compared morbidity within 60 days after SBTS and ES for left-sided malignant colonic obstruction. Based on the literature available at the time the study was conceived, reduced morbidity was expected after SBTS. Our

findings show that the two strategies are equivalent, that there were no differences in oncological outcomes at a median follow-up of 36 months, and that the stoma rate was markedly lower in the SBTS group. Furthermore, considering that up to 30% of temporary stomas are never reversed, the quality of life in these patients will be reduced. Taken together, the results of our study indicate that SBTS, when performed in expert hands, is a viable endoscopic approach to elective surgery for malignant colonic obstruction.

Acknowledgements The present study received endorsement by the European Association for Endoscopic Surgery.

Compliance with ethical standards

Disclosures Drs. Alberto Arezzo, Carmen Balague, Eduardo Targarona, Felice Borghi, Giorgio Giraudo, Luigi Ghezzo, Antonio Arroyo, Javier Sola-Vera, Paolo De Paolis, Maurizio Bossotti, Elisa Bannone, Edoardo Forcignanò, Marco Augusto Bonino, Roberto Passera, and Mario Morino have no conflicts of interest or financial ties to disclose.

References

1. Gandrup P, Lund L, Balslev I (1992) Surgical treatment of acute malignant large bowel obstruction. Eur J Surg 158:427–430
2. Mauro MA, Koehler RE, Baron TH (2000) Advances in gastrointestinal intervention: the treatment of gastroduodenal and colorectal obstructions with metallic stents. Radiology 215:659–669
3. Dohomoto M (1991) New method-endoscopic implantation of rectal stent in palliative treatment of malignant stenosis. Endosc Dig 3:1507–1512
4. Tejero E, Mainar A, Fernandez L, Tieso A, San Jose A (1995) New procedure for relief of malignant obstruction of the left colon. Br J Surg 82:34–35
5. Knight AL, Trompetas V, Saunders MP, Anderson HJ (2012) Does stenting of left-sided colorectal cancer as a "bridge to surgery" adversely affect oncological outcomes? A comparison with non-obstructing elective left-sided colonic resections. Int J Colorectal Dis 27:1509–1514
6. Sabbagh C, Browet F, Diouf M, Cosse C, Brehant O, Bartoli E, Mauvais F, Chauffert B, Dupas JL, Nguyen-Khac E, Regimbeau JM (2013) Is stenting as "a bridge to surgery" an oncologically safe strategy for the management of acute, left-sided, malignant, colonic obstruction? A comparative study with a propensity score analysis. Ann Surg 258:107–115
7. Dindo D, Demartines N, Clavien PA (2004) Classification of surgical complications. a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240:205–213
8. van Hooft JE, Bemelman WA, Oldenburg B, Marinelli AW, Lutke Holzik MF, Grubben MJ et al (2011) Colonic stenting versus emergency surgery for acute left-sided malignant colonic obstruction: a multicentre randomised trial. Lancet Oncol 12:344–352
9. Alcántara M, Serra-Aracil X, Falcó J, Mora L, Bombardó J, Navarro S (2011) Prospective, controlled, randomized study of intraoperative colonic lavage versus stent placement in obstructive left-sided colonic cancer. World J Surg 35:1904–1910
10. Tung KLM, Cheung HYS, Ng LWC, Chung CCC, Li MKW (2013) Endo-laparoscopic approach versus conventional open surgery in the treatment of obstructing left-sided colon cancer: long-term follow-up of a randomized trial. Asian J Endosc Surg 6:78–81
11. Sloothaak DAM, van den Berg MW, Dijkgraaf MGW, Fockens P, Tanis PJ, van Hooft JE et al (2014) Oncological outcome of malignant colonic obstruction in the Dutch Stent-In 2 trial. Br J Surg 101:1751–1757
12. Ansaloni L, Andersson RE, Bazzoli F, Catena F, Cennamo V, Di Saverio S et al (2010) Guidelines in the management of obstructing cancer of the left colon: consensus conference of the world society of emergency surgery (WSES) and peritoneum and surgery (PnS) society. World J Emerg Surg WJES 28(5):29
13. Al Samaraee A, McCallum IJ, Kenny L, Isreb S, Macdougall L, Hayat M et al (2011) Colorectal stents: do we have enough evidence? Int J Surg Lond Engl 9:595–599
14. Bonin EA, Baron TH (2010) Update on the indications and use of colonic stents. Curr Gastroenterol Rep 12:374–382
15. Cennamo V, Luigiano C, Coccolini F, Fabbri C, Bassi M, De Caro G et al (2013) Meta-analysis of randomized trials comparing endoscopic stenting and surgical decompression for colorectal cancer obstruction. Int J Colorectal Dis 28:855–863
16. Kim MK, Kye B-H, Lee IK, Oh ST, Ahn CH, Lee YS et al (2016) Outcome of bridge to surgery stenting for obstructive left colon cancer. ANZ J Surg 23:1867–1874
17. SCOTIA study group (1995) Single-stage treatment for malignant left-side colonic obstruction: a prospective randomized clinical trial comparing subtotal colectomy with segmental resection following intraoperative irrigation. Br J Surg 82:1622–1627
18. van Hooft JE, van Halsema EE, Vanbiervliet G, Beets-Tan RGH, DeWitt JM, Donnellan F et al (2014) Self-expandable metal stents for obstructing colonic and extracolonic cancer: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Gastrointest Endosc 80:747–761
19. De Ceglie A, Filiberti R, Baron TH, Ceppi M, Conio M (2013) A meta-analysis of endoscopic stenting as bridge to surgery versus emergency surgery for left-sided colorectal cancer obstruction. Crit Rev Oncol Hematol 88:387–403