Original article

Cost-effectiveness of sigmoid resection with primary anastomosis or end colostomy for perforated diverticulitis: an analysis of the randomized Ladies trial

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Background: **Several studies have been published favouring sigmoidectomy with primary anastomosis over Hartmann's procedure for perforated diverticulitis with purulent or faecal peritonitis (Hinchey grade III or IV), but cost-related outcomes were rarely reported. The present study aimed to evaluate costs and cost-effectiveness within the DIVA arm of the Ladies trial.**

Methods: **This was a cost-effectiveness analysis of the DIVA arm of the multicentre randomized Ladies trial, comparing primary anastomosis over Hartmann's procedure for Hinchey grade III or IV diverticulitis. During 12-month follow-up, data on resource use, indirect costs (Short Form Health and Labour Questionnaire) and quality of life (EuroQol Five Dimensions) were collected prospectively, and analysed according to the modified intention-to-treat principle. Main outcomes were incremental cost-effectiveness (ICER) and cost–utility (ICUR) ratios, expressed as the ratio of incremental costs and the incremental probability of being stoma-free or incremental quality-adjusted life-years respectively.**

Results: **Overall, 130 patients were included, of whom 64 were allocated to primary anastomosis (46 and 18 with Hinchey III and IV disease respectively) and 66 to Hartmann's procedure (46 and 20 respectively). Overall mean costs per patient were lower for primary anastomosis (€20 544, 95 per cent c.i. 19 569 to 21 519) than Hartmann's procedure (€28 670, 26 636 to 30 704), with a mean difference of €−8126 (−14 660 to −1592). The ICER was €−39 094 (95 per cent bias-corrected and accelerated (BCa) c.i. −1213 to −116), indicating primary anastomosis to be more cost-effective. The ICUR was €−101 435 (BCa c.i. −1 113 264 to 251 840).**

Conclusion: **Primary anastomosis is more cost-effective than Hartmann's procedure for perforated diverticulitis with purulent or faecal peritonitis.**

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Introduction

Acute diverticulitis is a common diagnosis in developed countries that is associated with considerable healthcare costs[1–5]. The incidence of perforated diverticulitis with purulent or faecal peritonitis (Hinchey grade III or IV) is increasing, emphasizing the need for cost-effective emergency surgical management[6,7].

In recent years, results have been published favouring sigmoidectomy with primary anastomosis (PA) over Hartmann's procedure (HP) for the treatment of Hinchey III and IV diverticulitis[8]. Benefits of PA comprise lower short-term morbidity rates after index and reversal procedures, as well as a higher rate of stoma-free survival, shorter time to stoma reversal and shorter postreversal hospital stay[8–11]. Although these outcomes might reduce associated costs, studies comparing the two treatment strategies in terms of related costs and cost-effectiveness are scarce. Therefore, a cost-effectiveness analysis was undertaken comparing PA (with or without defunctioning ileostomy) with HP in patients treated in the DIVA arm of the Ladies trial[11,12].

Methods

This cost-effectiveness analysis was conducted within the DIVA arm of the Ladies trial. The study protocol, including details of cost analyses and clinical outcomes, has been reported previously[11,12]. In summary, the Ladies trial was an international, multicentre, parallel-group, randomized, open-label superiority trial of the surgical management of perforated diverticulitis. The aim of the DIVA arm was to compare HP and PA (with or without defunctioning ileostomy) as treatment for Hinchey III or IV diverticulitis. After diagnostic laparoscopy, patients were assigned randomly to HP or PA in a 1 : 1 ratio. Patients with dementia, a history of sigmoidectomy or pelvic radiotherapy, chronic steroid treatment (at least 20 mg daily) or preoperative shock requiring inotropic support were excluded. The primary endpoint of the DIVA arm was 12-month stoma-free survival and secondary outcomes (such as morbidity and readmissions) were also recorded. The study was registered at trialregister.nl (NTR2037) and ClinicalTrials.gov (NCT01317485), and designed in accordance with the Declaration of Helsinki and good clinical practice guidelines. The study protocol was approved by the ethical review board, and written informed consent was obtained from all patients before randomization. The CHEERS guidelines and checklist[13] were used as guidance for the present cost-effectiveness analysis.

Economic evaluation

The present analysis aimed to assess the cost-effectiveness and cost–utility of HP compared with PA during the first 12 months after the index procedure, and included both direct and indirect costs (medical and non-medical). The economic evaluation was performed from a societal perspective, and in accordance with the guidelines for health economic analyses published by the Dutch National Health Care Institute[14].

Resource use

Data on resource use were collected prospectively through clinical record forms and study questionnaires completed 1, 3, 6, 9 and 12 months after the index procedure. Direct medical costs were those related to index and stoma reversal surgery and related admissions (such as ward and ICU stay), reinterventions (acute relaparotomy or percutaneous drainage), additional diagnostic imaging (X-ray, ultrasound imaging, CT), readmissions, stoma care, emergency department visits, and outpatient consultation visits with the surgeon, gastroenterologist, general practitioner or company physician. Costs of the index procedure actually performed were used and did not include the cost of the study protocol-based diagnostic laparoscopy. Costs associated with home and informal care and travel expenses were considered as direct non-medical costs. Indirect non-medical costs resulting from work absence or decreased productivity were determined by use of the Short Form Health and Labour Questionnaire (SF-HLQ)[15]. To estimate loss of productivity, the friction costs method was used with age-adjusted mean daily wages derived from the Dutch National Health Care Institute guideline[14]. Total costs per patient were calculated by multiplying resources used by associated unit costs.

Quality-adjusted life-years

Health-related quality of life (QoL) and quality-adjusted life-years (QALYs) were derived from the EuroQol Five Dimensions three-level questionnaire (EQ-5D-3 L™; EuroQol Group, Rotterdam, the Netherlands) at 2 and 4 weeks, 3, 6 and 12 months after the index procedure. Outcomes were scored from 0 to 1 according to the Dutch EQ-5D™ tariff, where 1 is considered to represent optimal QoL.

Unit costs

Unit costs were calculated according to the methods described by Vennix and colleagues[16], and were estimated based on top-down cost calculations from the hospital costs ledger of the Amsterdam University Medical Centre and Dutch guideline on unit costing in healthcare[17]. Moreover, bottom-up cost calculations for laparoscopic and open sigmoidectomy with and without PA were performed, including costs of instruments (reusable and disposable), and costs of personnel and overheads per time unit. As the index procedures and Hartmann's reversal procedures could be open or laparoscopic, mean costs were calculated taking the ratio of these different possible procedures into account. Costs were calculated in euros, adjusted to 2018 by the Dutch consumer price index.

Statistical analysis

Depending on data distribution, continuous variables are presented as median (i.q.r.) or mean(s.d.). Categorical variables are shown as numbers with percentages. Patients were analysed according to the modified intention-to-treat principle, with costs calculated based on the index procedure actually performed. The intention-to-treat approach was deemed modified owing to the exclusion of three patients shortly after randomization who were found to have alternative diagnoses[11]. The bias-corrected and accelerated (BCa) bootstrapping method (1000 samples) was used to calculate 95 per cent confidence intervals[18]. Missing data on EQ-5D™ values and indirect costs were imputed by means of multiple imputation, taking into account age, sex, Hinchey grade, randomization and direct costs. Imputed data were pooled according to Rubin's rule[19].

To determine the robustness of the calculated costs, sensitivity analyses were performed by varying unit costs of resources used (direct medical costs). Incremental cost-effectiveness (ICER) and cost–utility (ICUR) ratios were calculated as the mean difference between treatment groups in total costs per patient divided by the mean difference in probability of being stoma-free and mean difference in QALYs respectively. Cost-effectiveness planes and acceptability curves were derived. Analyses were performed using SPSS® version 24.0 (IBM, Armonk, New York, USA) and R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Between 1 July 2010 and 22 February 2013, and between 9 June 2013 and 6 June 2016, patients could be included in the DIVA arm of the Ladies trial. Trial inclusion was temporarily paused, owing to the early termination of the LOLA arm of the study. Eventually, a total of 130 patients were included according to a modified intention-to-treat principle, of whom 66 were analysed in the HP group and 64 in the PA group. One patient in the PA group was lost to follow-up after 30 days (*Fig. S1*, supporting information). All patients were included in the present cost evaluation. Baseline and operative characteristics are summarized in *Table 1*. Full trial details and outcomes have been published previously[11]. Response rates to the SF-HLQ questionnaires are documented in *Table S1* (supporting information).

Table 1 Summary of baseline and operative characteristics

	Hartmann's procedure (*n* = 66)	Primary anastomosis (*n* = 64)
Patient characteristics		
Age (years)*	61·7(11·4)	62·4(13·1)
Sex ratio (F : M)	25 : 41	23 : 41
BMI (kg/m²)*	28·0(4·7)	26·3(4·8)
ASA fitness grade		
I–II	37 (63)	45 (76)
III–IV	22 (37)	14 (24)
Missing	7	5
Hinchey grade IV	20 (30)	18 (28)
Operative characteristics		
Laparoscopic lavage	0	1 (2)
Hartmann's procedure	65 (98)	7 (11)
Primary anastomosis	1 (2)	56 (88)
Stoma		
No	1 (2)	18 (28)
Yes	65 (98)	46 (72)
Duration of surgery (min)†	118 (96–135)	125 (110–154)
Laparoscopic procedure	20 (30)	17 (27)

Values in parentheses are percentages unless indicated otherwise; values are *mean(s.d.) and †median (i.q.r.).

Table 2 Major resources and unit costs

	Mean cost (€)	Unit
Hartmann's procedure	3247	Procedure
Primary anastomosis	3914	Procedure
Laparoscopic lavage	2346	Procedure
Ileostomy reversal	2655	Procedure
Colostomy reversal	4087	Procedure
Acute relaparotomy	3476	Procedure
Percutaneous drainage	14	Procedure
Elective sigmoid resection	4266	Procedure
Incisional hernia repair	1305	Procedure
Surgical ward stay	419	Day
ICU stay	2084	Day

Values are indexed for 2018.

Costs and resource use

A summary of unit costs of major resources is provided in *Table 2*, with full details in *Table S2* (supporting information). Resource use and calculated costs are shown in *Table 3*. Stoma-related costs were significantly higher in the HP group (€8372, 95 per cent c.i. 7316 to 9429) than in the PA group (€4382, 3481 to 5284), with a mean difference of €−3990 (−5370 to −2611). Overall total costs were €1 892 206 for the HP group and €1 314 798 for the PA group. Mean costs per patient were €28 670 (26 636 to 30 704) and €20 544 (19 569 to 21 519) respectively. This amounted to a mean difference in costs of €−8126 (−14 660 to −1592) in favour of PA.

Cost-effectiveness and cost–utility

The mean probability of being stoma-free at end of the 12-month follow-up was 86 (95 per cent c.i. 74 to 93)

Table 3 Resource use and costs

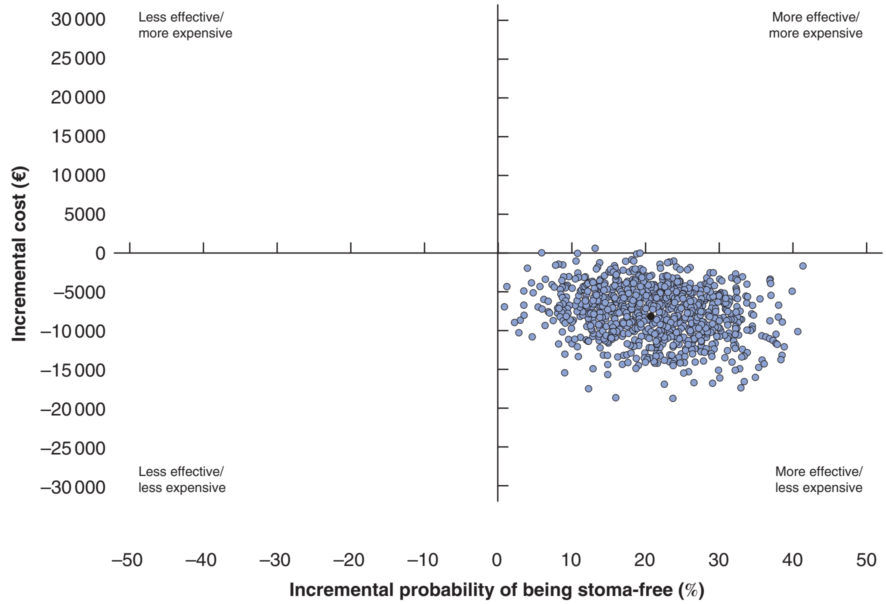
	Unit	Hartmann's procedure (*n* = 66)		Primary anastomosis (*n* = 64)	
		Total units	Total costs (€)	Total units	Total costs (€)
Index admission					
Hartmann's procedure	Procedure	65	211 083	7	22 732
Primary anastomosis	Procedure	1	3914	56	219 181
Laparoscopic lavage	Procedure	0	0	1	2346
Surgical ward	Day	733	307 076	591	247 588
Intensive care unit	Day	197	410 611	87	181 336
Additional imaging	Test	264	31 039	159	21 448
Subtotal			963 723		694 630
Mean subtotal per patient			14 602 (8514, 20 689)		10 854 (9126 to 12 581)
Mean difference in subtotal			−3748 (−10 101, 2604)		
Readmissions and reinterventions					
Acute reinterventions	Procedure	18	31 064	12	28 154
Elective reinterventions	Procedure	4	5218	1	1305
Readmission to surgical ward	Day	172	72 056	142	59 488
Readmission intensive care unit	Day	0	0	0	0
Subtotal			108 339		88 946
Mean subtotal per patient			1641 (626, 2657)		1390 (677, 2102)
Mean difference in subtotal			−252 (−1488 to 984)		
Stoma-related costs					
Stoma care	Day	13 118	245 965	8288	104 737
Reversal surgery	Procedure	45	183 915	38	106 612
Reversal admission (surgical ward + ICU)	Day	277	122 705	165	69 123
Subtotal			552 584		280 473
Mean subtotal per patient			8372 (7316, 9429)		4382 (3481, 5284)
Mean difference in subtotal			−3990 (−5370, −2611)		
Other costs					
Ìmaging	Test	64	9282	38	4811
Consultations and travel expenses	Visit	349	30 038	295	26 423
Total direct medical costs			1 663 966		1 095 283
Indirect non-medical costs			228 240		219 515
Total costs (12 months)			1 892 206		1 314 798
Mean cost per patient			28 670 (26 636, 30 704)		20 544 (19 569, 21 519)
Mean difference in costs			−8126 (−14 660, −1592)		

Values in parentheses are 95 per cent confidence intervals. Mean costs are shown, indexed for 2018. Smaller cost groups (such as hospital and general practitioner visits) are included in (sub)total costs.

per cent for the PA group and 65 (53 to 75) for the HP group, with a significant mean difference of 21 (7 to 36) per cent. *Fig. 1* shows a cost-effectiveness plane, indicating the relationship between incremental costs and the incremental probability of being stoma-free and alive. The ICER was €−39 094 (95 per cent BCa c.i. −1213 to −116), indicating that PA was more cost-effective than HP. The associated willingness-to-pay curve is shown in *Fig. S2* (supporting information).

The mean value of QALYs during the 12-month follow-up was 0·72 (95 per cent c.i. 0·69 to 0·76) in the PA group, compared with 0·64 (0·60 to 0·68) in the HP group. The mean difference in QALYs was 0·08 (−0·03 to 0·19), which was not statistically significant. The ICUR was €−101 435 (95 per cent BCa c.i. −1 113 264 to 251 840). A cost–utility plane and willingness-to-pay curve are shown in *Fig. 2* and *Fig. S3* (supporting information) respectively.

Fig. 1 Cost-effectiveness plane



Black dot indicates the point estimate upon which the 1000 bootstrap samples are based.

Table 4 Sensitivity analyses of medical costs

	Hartmann's procedure (€)	Primary anastomosis (€)	Cost difference (€)
Total medical costs (base-case analysis)	25 212 (21 251, 34 132)	17 114 (15 297, 19 636)	−8098 (−17 016, −3550)
Index surgery			
−50%	23 583 (19 603, 32 482)	15 206 (13 398, 17 789)	−8377 (−17 214, −3818)
+50%	26 840 (22 847, 37 381)	19 022 (16 978, 21 455)	−7818 (−18 129, −3269)
Hospital stay (ward, ICU)			
−20%	23 036 (19 258, 30 896)	15 773 (14 139, 17 939)	−7263 (−14 878, −2910)
+20%	27 386 (22 398, 39 156)	18 454 (16 284, 21 358)	−8932 (−19 534, −3261)
Stoma-associated costs			
−20%	23 537 (19 566, 33 672)	16 237 (14 598, 18 812)	−7300 (−16 843, −2507)
+20%	26 886 (22 880, 35 540)	17 990 (16 064, 20 586)	−8896 (−17 734, −4320)
Acute or elective reintervention			
−20%	25 102 (21 174, 35 659)	17 022 (15 370, 19 443)	−8079 (−18 375, −3742)
+20%	25 321 (21 399, 36 105)	17 206 (15 499, 19 746)	−8116 (−18 526, −3742)

Values in parentheses are 95 per cent confidence intervals.

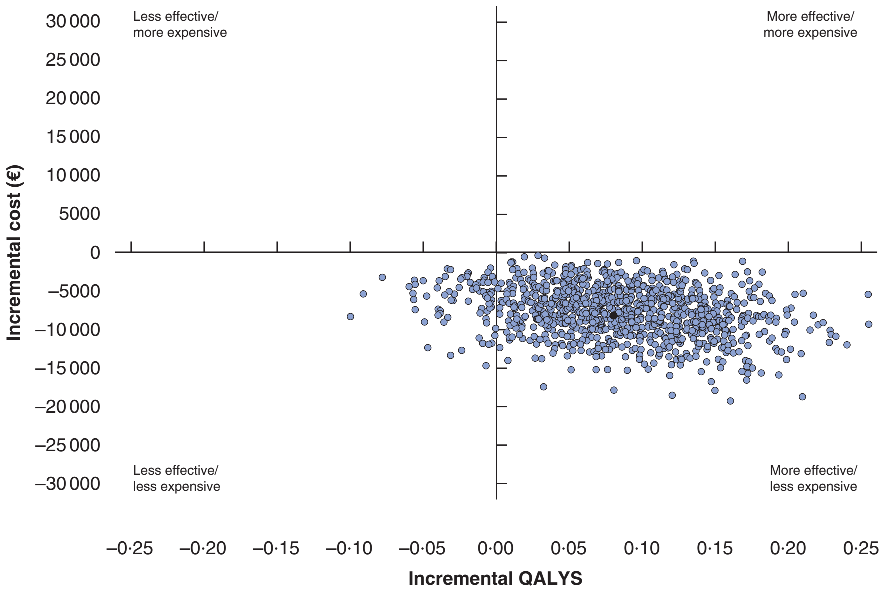
Sensitivity analyses

Table 4 shows the results of sensitivity analyses, in which unit costs for specified cost groups were increased and decreased by 20 or 50 per cent, while those for other cost groups were not changed. Overall, these results demonstrated that PA was associated with lower costs, with cost differences ranging from €−7263 to €−8932.

Discussion

Admission rates for diverticulitis have increased over the past few decades[6,20–23] and the incidence of perforated disease, for which surgery is often needed, has risen[24–26]. In a retrospective study[27], overall expenses were between 74 and 229 per cent higher for HP than PA. More recently[28], in-hospital costs within an RCT were found to be higher for HP, but this was not statistically significant. The present

Fig. 2 Cost–utility plane



Black dot indicates the point estimate upon which the 1000 bootstrap samples are based. QALY, quality-adjusted life-year.

study differed from previous analyses by capturing all costs prospectively, including indirect non-medical and other resource expenses (such as those related to readmissions or outpatient department visits) over the full 12-month follow-up. It showed that PA was more cost-effective in the first postoperative year and in terms of the probability of being stoma-free. Advantages of PA derive from a shorter time to, and less morbidity after, stoma reversal, and a shorter hospital stay, which are likely to reduce costs[11]. Indeed, a large difference in absolute stoma-related costs was identified in favour of PA. This is in line with a cost-effectiveness analysis of the LOLA arm of the Ladies trial[16], in which stoma-related costs were higher for resection than laparoscopic lavage for Hinchey III diverticulitis, and the economic analysis of the related DILALA (DIverticulitis – LAparoscopic LAvage *versus* resection (Hartmann's procedure) for acute diverticulitis with peritonitis) study[29].

In terms of generalizability, some aspects are of importance to consider when interpreting the present outcomes. The majority of patients included in the Ladies trial were Dutch[11], and unit costs and subsequent calculations are based on that healthcare system. The results should be interpreted within the context of the inclusion and exclusion criteria that applied to the DIVA arm. Therefore, strictly speaking, the present outcomes apply only to haemodynamically stable, immunocompetent patients aged less than 85 years[11]. Enrolment was terminated early because of slow accrual. Although not uncommon for RCTs in the emergency setting[30], early termination may limit the sample size and statistical power. The study was not specifically powered to show differences in cost-associated or patient-reported outcomes. Hence, it was decided not to differentiate between Hinchey III and IV diverticulitis in the present study, as this would have further reduced group sizes. In spite of the sample size, significant differences in overall mean costs per patient were identified, and their robustness was demonstrated in sensitivity analyses. Another limitation was the response rate to the questionnaires sent out during follow-up, which ranged from 47 to 64 per cent. Multiple imputation techniques were used to handle missing data and to decrease the influence of potential attrition bias.

This study has several strengths, including the setting of a multicentre randomized trial with cost data collected prospectively from a societal perspective, and indirect non-medical costs (such as absence from work and productivity losses) taken into account. These factors are relevant to consider as the disease is increasingly being seen in younger patients of working age[20,21,23]. The assessment of unit costs came from the hospital ledger and Dutch costing manual[14], rather than being derived from diagnosis-related group data, to better reflect clinical practice at a more individual level.

In general, the treatment of diverticulitis has shifted towards less aggressive approaches, which might also have beneficial effects on associated costs[31]. The avoidance of antibiotics for uncomplicated diverticulitis has been proven to be safe in both the short and long term[32–35]. The role of percutaneous drainage for diverticulitis with abscess formation has been debated[36,37]. Subsequently, follow-up without elective colectomy after non-operative treatment of an initial episode of diverticulitis with abscess formation or local extraluminal air seems justified[38,39]. Moreover, evidence shows that HP for perforated diverticulitis should be avoided if possible and that PA is preferred[9–11]. The present cost-effectiveness analysis has provided a health economic argument for use of PA over HP for perforated diverticulitis.

Collaborators

Members of the Ladies trial who collaborated in this study: Study design: J. Vermeulen (Department of Surgery, Maasstad Hospital, Rotterdam); W. C. Hop (Department of Epidemiology, Erasmus University Medical Centre, Rotterdam); B. C. Opmeer (Clinical Research Unit, Amsterdam University Medical Centre, AMC, Amsterdam); J. B. Reitsma (Julius Centre for Health Sciences, University Medical Centre Utrecht, Utrecht). Randomization management: R. A. Scholte, E. W. H. Waltmann (Clinical Research Unit, Amsterdam University Medical Centre, AMC, Amsterdam). Data Safety Monitoring Board: D. A. Legemate (Department of Surgery, Amsterdam University Medical Centre, AMC, Amsterdam); J. F. Bartelsman (Department of Gastroenterology, Amsterdam University Medical Centre, AMC, Amsterdam); D. W. Meijer (Department of Surgery, Amsterdam University Medical Centre, VUmc, Amsterdam); J. B. Reitsma (Julius Centre for Health Sciences, University Medical Centre Utrecht, Utrecht). Investigators and participating surgeons/residents of the DIVA arm; Netherlands: W. A. Bemelman, S. Vennix, G. D. Musters, H. A. Swank, Ç. Ünlü, A. B. Kluit, Y. El-Massoudi, R. J. C. L. M. Vuylsteke, P. J. Tanis, R. Matthijsen, S. W. Polle, S. M. Lagarde, S. S. Gisbertz, O. Wijers, J. D. W. van der Bilt, M. A. Boermeester, R. Blom, J. A. H. Gooszen, M. H. F. Schreinemacher, T. van der Zande, M. M. N. Leeuwenburgh (Department of Surgery, Amsterdam University Medical Centre, AMC, Amsterdam); J. A. B. van der Hoeven, S. A. L. Bartels, W. L. E. M. Hesp, L. Koet (Department of Surgery, Albert Schweitzer Hospital, Dordrecht); R. M. P. H. Crolla, G. P. van der Schelling, E. van Dessel, M. L. P. van Zeeland, M. M. A. Lensvelt, H. Nijhof, S. Verest, M. Buijs, J. H. Wijsman (Department of Surgery, Amphia Hospital, Breda); L. P. S. Stassen, M. Klinkert, M. F. G. de Maat, G. Sellenraad (Department of Surgery, Academic Hospital Maastricht, Maastricht); J. F. Lange, I. M. Mulder, J. Jeekel, G. J. Kleinrensink, T. Tha-In, W. N. Nijboer (Department of Surgery, Erasmus University Medical Centre, Rotterdam); M. J. Boom, P. C. M. Verbeek (Department of Surgery, Flevo Hospital, Almere); P. M. Kruyt, C. Sietses, M. W. J. Stommel (Department of Surgery, Gelderse Vallei Hospital, Ede); W. H. Steup, P. J. van Huijstee, J. W. S. Merkus, D. Eefting, J. S. D. Mieog (Department of Surgery, Haga Hospital, The Hague); E. G. J. M. Pierik, D. van Geldere, G. A. Patijn, M. de Vries, M. Boskamp (Department of Surgery, Isala Hospital, Zwolle); H. B. A. C. Stockmann, Q. A. J. Eijsbouts, A. Bentohami, T. S. Bijlsma, N. de Korte, D. Nio, H. Rijna, J. Luttikhold, M. H. van Gool, J. F. Fekkes, G. J. M. Akkersdijk, G. Heuff, E. H. Jutte, B. A. Kortmann, J. M. Werkman, W. Laméris, L. Rietbergen, P. Frankenmolen (Department of Surgery, Spaarne Gasthuis, Haarlem); E. C. J. Consten, W. A. Draaisma, M. A. W. Stam, M. S. Verweij (Department of Surgery, Meander Medical Centre, Amersfoort); M. F. Gerhards, B. A. van Wagensveld, T. M. Karsten, H. Rijna, L. C. de Nes, S. Fortuin, S. M. De Castro, A. Doeksen, M. P. Simons, G. I. Koffeman, E. P. Steller, J. B. Tuynman, P. Boele van Hensbroek, M. Mok, S. R. van Diepen (Department of Surgery, OLVG, Amsterdam); A. G. M. Hoofwijk, H. J. Belgers, K. W. E. Hulsewé, J. Melenhorst, J. H. M. B. Stoot, S. Fransen, M. N. Sosef, J. van Bastelaar, Y. L. J. Vissers, T. P. D. Douchy, C. E. Christiaansen, R. Smeenk, A. M. Pijnenburg, V. Tanaydin, H. T. C. Veger, S. H. E. M. Clermonts, M. Al-Taher (Department of Surgery, Zuyderland Medical Centre, Sittard-Geleen); E. J. R. de Graaf, A. G. Menon, M. Vermaas (Department of Surgery, IJsselland Hospital, Capelle aan den IJssel); H. A. Cense, E. Jutte (Department of Surgery, Rode Kruis Hospital, Beverwijk); T. M. Karsten, M. Vermaas (Department of Surgery, Reinier de Graaf Hospital, Delft); M. J. Wiezer, A. B. Smits (Department of Surgery, St Antonius Hospital, Nieuwegein); A. A. W. van Geloven, M. Westerterp, H. A. Marsman, E. R. Hendriks, O. van Ruler, E. J. C. Vriens, J. M. Vogten, C. C. van Rossem, D. Ohanis, E. Tanis, J. van Grinsven (Department of Surgery, Tergooi Hospital, Hilversum); J. K. Maring, J. Heisterkamp (Department of Surgery, Elisabeth-TweeSteden Hospital, Tilburg); W. M. U. van Grevenstein, M. R. Vriens, M. G. H. Besselink, I. H. M. Borel Rinkes, I. Q. Molenaar (Department of Surgery, University Medical Centre, Utrecht); M. J. P. M. Govaert, J. J. A. Joosten, V. Jongkind, G. M. P. Diepenhorst, M. C. Boute, M. Smeenge, K. Nielsen, J. J. Harlaar (Department of Surgery, Dijklander Hospital, Hoorn); S. W. Nienhuijs, M. D. P. Luyer, G. van Montfort, J. F. Smulders, F.

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Supporting information

Additional supporting information can be found online in the Supporting Information section at the end of the article.