European Journal of Surgical Oncology 49 (2023) 106968

Contents lists available at ScienceDirect

European Journal of Surgical Oncology

journal homepage: www.ejso.com

Cost analysis of robot-assisted versus open transthoracic esophagectomy for resectable esophageal cancer. Results of the ROBOT randomized clinical trial☆

Lucas Goense [a, *], Pieter C. van der Sluis [a, b], Sylvia van der Horst [a], Evangelos Tagkalos [b], Peter P. Grimminger [b], Wouter van Dijk [c], Jelle P. Ruurda [a], Richard van Hillegersberg [a, **]

[a] Department of Surgery, University Medical Center Utrecht, Utrecht, the Netherlands
[b] Department of General-, Visceral- and Transplant Surgery, University Medical Center of the Johannes Gutenberg University, Mainz, Germany
[c] MRDM, the Netherlands

ARTICLE INFO

Article history:
Received 22 June 2022
Received in revised form
9 May 2023
Accepted 22 June 2023
Available online 01 July 2023

Keywords:
Esophageal cancer
Esophagectomy
RAMIE
MIE
Healthcare costs

ABSTRACT

Background: The previously published ROBOT trial demonstrated that robot assisted minimally invasive esophagectomy (RAMIE) is associated with a lower percentage of postoperative complications compared to open esophagectomy (OTE) for patients with esophageal cancer. The implications of these results on healthcare costs are important given the increased attention for cost-reduction in healthcare. Therefore the aim of this study was to report the hospital costs of RAMIE compared to OTE as treatment for esophageal cancer.
Methods: The ROBOT trial randomized 112 patients with esophageal cancer between RAMIE and OTE through January 2012 and August 2016 in a single tertiary care academic centre in the Netherlands. The primary outcome of the current study was hospital costs from the day of esophagectomy until 90 days after discharge based on Time-Driven Activity-Based Costing methodology. Secondary outcomes included the incremental cost-effectiveness ratio per complication prevented and risk factors for increased hospital costs.
Results: Of the 112 included patients, 109 patients underwent an esophagectomy, of whom 54 RAMIE and 55 OTE. The mean total hospital costs were comparable between RAMIE €40211 and OTE €39495 (mean difference €-715; bias-corrected and accelerated confidence interval € −14831 to 14783, $p = 0.932$). At a willingness-to-pay threshold of €20.000 to €25.000 (i.e. estimated additional costs to the hospital to treat patients with a complication) RAMIE had a probability 62%–70% of being cost effective to prevent postoperative complications. In multivariable regression analysis, major postoperative complications were the main driver of hospital costs after esophagectomy (€31839, $p = 0.009$).
Conclusion: In this randomized trial RAMIE resulted in fewer postoperative complications compared to OTE without increasing total hospital costs.

1. Introduction

In a recent randomized controlled trial (ROBOT trial, NCT01544790) robot assisted minimally invasive esophagectomy (RAMIE) was compared to open transthoracic esophagectomy (OTE) as a treatment for esophageal cancer [1,2]. RAMIE was associated with a significant lower percentage of overall surgery-related postoperative complications, less cardiopulmonary complications, less blood loss, lower postoperative pain with better functional recovery and improved short-term quality of life [2]. Oncologic outcomes, such as the percentage of radical (R0) resections, the number of resected lymph nodes and disease-free and overall survival were comparable between both groups and in concordance with large clinical trials [3].

☆ This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.
* Corresponding author. Department of Surgery, University Medical Centre Utrecht Heidelberglaan 100, 3584 CX, Utrecht, the Netherlands.
** Corresponding author.
E-mail addresses: l.goense@umcutrecht.nl (L. Goense), r.vanhillegersberg@umcutrecht.nl (R. van Hillegersberg).

https://doi.org/10.1016/j.ejso.2023.06.020
0748-7983/

However, robotic assisted surgery is associated with increased material costs compared to open surgery due to high costs of the acquisition of a robotic system, maintenance costs, costs of disposable instruments and longer duration of surgery [4]. On the other hand, it was previously shown that complications and severity of complications after esophageal surgery are associated with a substantial increase in costs [5,6]. In the ROBOT-trial, RAMIE was associated with a lower incidence of complications compared to OTE [2]. Our hypothesis is that a reduction in complications and their associated costs may compensate the increased surgical costs associated with RAMIE compare to OTE. Until now, no hospital costs analyses have been performed for RAMIE compared to OTE in a randomized setting. Therefore, the aim of this study was to compare hospital costs after RAMIE and OTE for esophageal cancer from a previously randomized controlled trial (ROBOT-trial).

2. Methods

The rationale and design for the ROBOT trial and the primary endpoint results have been described previously [1]. In brief, patients with resectable esophageal cancer were randomized between either open transthoracic esophagectomy (OTE) or robot assisted minimally invasive esophagectomy (RAMIE). All surgical procedures were performed by the same surgeons in the UMC Utrecht (J.R. and R.H.) who performed at least 50 RAMIE and 50 OTE procedures each before the start of the trial. The inclusion and exclusion criteria, diagnostic workup, neoadjuvant treatment, pathologic examination, and postoperative management were described previously [2].

The primary outcome of the initial study was the occurrence of overall postoperative complications according to the Modified Clavien Dindo Classification (MCDC) 2−5 [7]. All outcomes were recorded daily and prospectively by the trial coordinators (P.S. and S.H.). Outcomes were discussed in a weekly multidisciplinary meeting, where the participants were unaware of treatment allocation. The medical ethics committee of the University Medical Center Utrecht approved the study. Written informed consent was obtained from all participating patients. After obtaining written informed consent, patients were randomized by the study coordinators separate from the surgeons who informed the patients for inclusion in the trial. Allocation of concealment was performed using computer generated random numbers in sealed opaque envelopes corresponding to either RAMIE or OTE. This article describes the costs analysis of the ROBOT trial.

3. Cost analysis

The cost analysis of the ROBOT-trial was conducted from a hospital perspective. The primary outcome was hospital costs from the day of esophagectomy until 90 days after discharge. The cost-effectiveness endpoint was the cost per complication prevented. Resource utilization was extracted from the hospital information system at a patient level (for example: operative costs including operation room time, ward and intensive care unit costs, radiology and laboratory costs) and translated into costs by Performation (Bilthoven, The Netherlands), which is a healthcare consultancy firm providing patient level costing. Time-Driven Activity-Based Costing (TD-ABC) methodology was used to calculate costs for esophagectomy, which is an improved approach for understanding hospital costs, as in incorporates both indirect (e.g. catering, cleaning and utilization of the hospital building) and direct costs (e.g. personnel staff, material and equipment; including costs of the robot) in this cost analysis [8]. All costs are presented in euros.

4. Statistical analysis

Analyses were performed according to an intention-to-treat principle, all patients who were scheduled for surgery after randomization were included. A sensitivity analysis was performed excluding patients in whom no formal resection was performed because irresectable disease was found intraoperatively. Further, a sensitivity analysis was performed in which the 5% most expensive patients were excluded to mitigate the effect of extreme cases. Summary statistics were used to describe patient and treatment-related characteristics. Categorical variables were presented as frequencies with percentages and continuous variables were presented as means with standard deviation (SD).

Differences in hospital costs were analysed by means of non-parametric bootstrapping, using 1000 samples of the same sizes as the original samples, with replacement. Mean differences are reported with corresponding 95% bias-corrected and accelerated confidence intervals (BCaCI) [9]. The relation between patient and treatment-related characteristics and complications with total costs was studied using multivariable linear regression with bootstrapping. Possible predictors were entered in the multivariable analysis when showing a near significant ($p < 0.20$) difference in costs according to the univariable analysis.

A cost-effectiveness analysis considers the difference of costs between two interventions (in this case RAMIE versus OTE) divided by the changes in outcome (i.e. difference in effect). An incremental cost-effectiveness ratio for RAMIE versus OTE was calculated as the difference in mean costs per patient divided by the mean risk reduction in complications. In this study the ratio represents the average incremental cost associated with the prevention of a complication after esophagectomy. Results of the cost-effectiveness analysis, using 1000 bootstrap samples, were presented using a cost-effectiveness plane and a cost-effectiveness acceptability curve to illustrate the uncertainty of sampling in the estimation of cost-effectiveness.

The cost-effectiveness acceptability curve shows the probability of RAMIE being cost-effective for different levels of willingness-to-pay values, ranging from 0 to larger thresholds. The willingness-to-pay thresholds can be determined as the amount of money the payer is willing to pay to obtain the outcome of interest (i.e. price per complication prevented). For the specific objective of estimating the cost effectiveness in this trial, it was hypothesised that healthcare providers would be willing to pay to prevent postoperative complications as long as it costs less than the treatment of a complication. According to two previously published studies from the Netherlands and Sweden, the average additional cost burden of any postoperative complicated course after esophagectomy ranged between €18500 and €22500 euro's [5,6]. Statistical analysis was performed using SPSS version 27.0 (IBM Corp., Armonk, NY). A p-value of <0.05 was considered statistically significant.

5. Results

5.1. Patients

In total, 112 patients were randomized to undergo either RAMIE or OTE. Prior to surgery 1 patient died during neoadjuvant treatment, 1 developed interval metastasis, and 1 patient physically deteriorated and refused surgery. In total 109 patients were planned for the randomized intervention (RAMIE $n = 54$ and OTE $n = 55$) and were included in the intention to treat analysis. Demographic and clinical baseline characteristics were comparable (Table 1). The primary endpoint, overall surgery related postoperative complications occurred in 32/54 (59%) patients after

Table 1
Characteristics of the RAMIE and OTE groups.

	RAMIE (n = 54)	OTE (n = 55)
Age (year)[¶]	64 (±8.9)	65 (±8.2)
Gender (n (%))		
Male	46 (85)	42 (76)
Female	8 (15)	13 (24)
BMI (kg/m^2)[¶†]	26.1 (±4.4)	25.5 (±4.7)
ASA score (n (%))[a]		
1	13 (24)	11 (20)
2	37 (69)	34 (62)
3	6 (11)	10 (18)
Type of carcinoma (n (%))		
Adenocarcinoma	41 (76)	43 (78)
Squamous cell carcinoma	13 (24)	12 (23)
Location of tumor (n (%))		
Upper third	1 (2)	0 (0)
Middle third	5 (9)	8 (15)
Lower third	26 (48)	29 (53)
Gastro-esophageal junction	22 (41)	18 (33)
Neoadjuvant treatment (n (%))		
Chemoradiotherapy	42 (79)	44 (80)
Chemotherapy	6 (11)	4 (7)
None	6 (11)	7 (13)
Tumor length (cm − range)[¶]	5.0 (±2.1)	4.4 (±1.8)
Clinical T stadium (n (%))		
cT1	5 (9)	6 (11)
cT2	11 (20)	7 (13)
cT3	37 (69)	41 (75)
cT4	1 (2)	1 (2)
Clinical N stadium (n (%))		
cTN0	15 (28)	19 (35)
cTN+	39 (72)	36 (65)
Any comorbidity (n (%))	43 (80)	41 (75)
Cardiac comorbidity	3 (6)	6 (11)
Vascular comorbidity	10 (19)	9 (17)
Pulmonal comorbidity	8 (15)	6 (11)
Thromboembolic comorbidity	20 (37)	19 (35)
Urological comorbidity	3 (6)	8 (15)
Neurological comorbidity	2 (4)	3 (5)
Previous operation (n (%))	22 (41)	18 (33)
History of malignancy (n (%))	15 (28)	16 (29)

¶Plus−minus values are means ± SD.
*modified Clavien-Dindo classification.
[a] ASA denotes American Society of Anesthesiologists.

RAMIE and in 44/55 (80%) patients after OTE (mean difference 21%, 95%CI 4%–36%). Detailed trial outcomes have been published previously [2]. In the RAMIE group, 2 patients were found to have irresectable disease intraoperatively and no formal resection was performed. An additional sensitivity analysis was performed excluding these two patients.

5.2. Cost analysis

Mean use of hospital resources and costs per patient for RAMIE and OTE, as well as mean cost differences, are shown in Table 2.

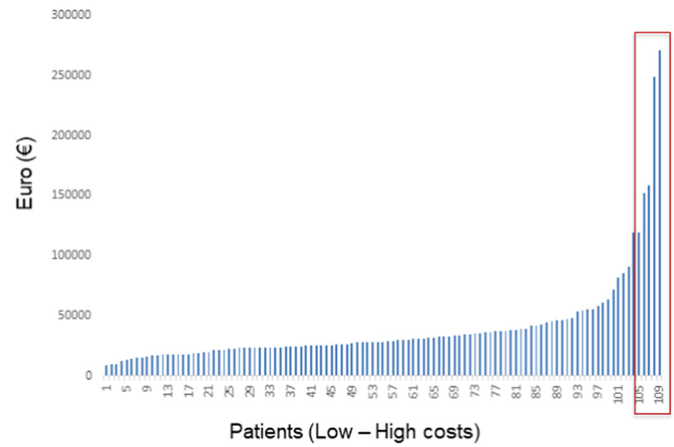

Fig. 1. For the entire cohort, the distribution of costs of all patients (n = 109), 4,5% of most expensive patients were responsible for 19.1% of all hospital costs.

Average costs of the initial surgical procedure were higher for RAMIE €8601 compared to OTE €5937 (mean difference € −2664, BCaCI € −4301 to € −1227, p = 0.004). However, the mean total hospital costs were comparable between RAMIE €40211 and OTE €39495 (mean difference €-715; BCaCI € −14831 to 14783, p = 0.932). Sensitivity analysis, excluding 2 patients in the RAMIE group with irresectable disease intraoperatively, demonstrated no difference in results. Also the sensitivity analysis excluding the 5% most expensive patients demonstrated no difference in healthcare costs between RAMIE and OTE (p = 0.406).

Differences in average intensive care unit costs, ward costs, laboratory costs, radiology costs and other costs between both groups did not reach statistical significance. Interestingly, the 5 (4,5%) most expensive patients in the entire cohort (2 robot, 3 open) were responsible for 19.1% of the total hospital costs assessed in this randomized controlled trial (Fig. 1). All these 5 patients suffered from an anastomotic leak leading to a sequela of other complications, reinterventions and a prolonged hospital stay, all contributing to high resource utilization.

5.3. Cost-effectiveness of postoperative complication prevention

The incremental cost-effectiveness ratio was EUR 715/0.21 = €3404 indicating the cost per prevented occurrence of a complication per patient by RAMIE. Fig. 2 demonstrates the difference in total hospital costs between RAMIE and OTE according to the % difference in prevented postoperative complications of the 1000 bootstrap samples. In 42.3% of bootstraps, hospital costs of RAMIE were lower and RAMIE resulted in less postoperative complications (lower right quadrant). In 55.4%, RAMIE was more expensive but resulted in less postoperative complications (upper

Table 2
Costs for the OTE and RAMIE groups (€).

	OTE (n = 55)	RAMIE (n = 54)	Difference in costs	P-value
Total costs	39495 (30611, 52032)	40211 (32001, 51580)	−715 (−14831, 14783)	0.932
Surgical costs	5937 (4825, 6996)	8601 (7479, 9933)	−2664 (−4301, −1227)	0.004
Intensive care unit costs	10965 (5553, 18740)	8917 (4458, 15895)	2048 (−7018, 12250)	0.700
Ward costs	13074 (10337, 16376)	13200 (10709, 15928)	−125 (−4327, 3830)	0.939
Laboratory costs	2771 (2106, 3638)	2558 (1935, 3287)	213 (−731, 1243)	0.699
Radiology costs	1801 (1433, 2258)	1769 (1435, 2148)	32 (-469–557)	0.887
Other costs[a]	4946 (3692, 6858)	5167(3935, 6542)	−220 (−2150, 1872)	0.832

[a] Other costs includes: other interventions; other diagnostics, blood productsValues are mean (95% bias-corrected and accelerated confidence intervals) costs estimated by non-parametric bootstrapping.

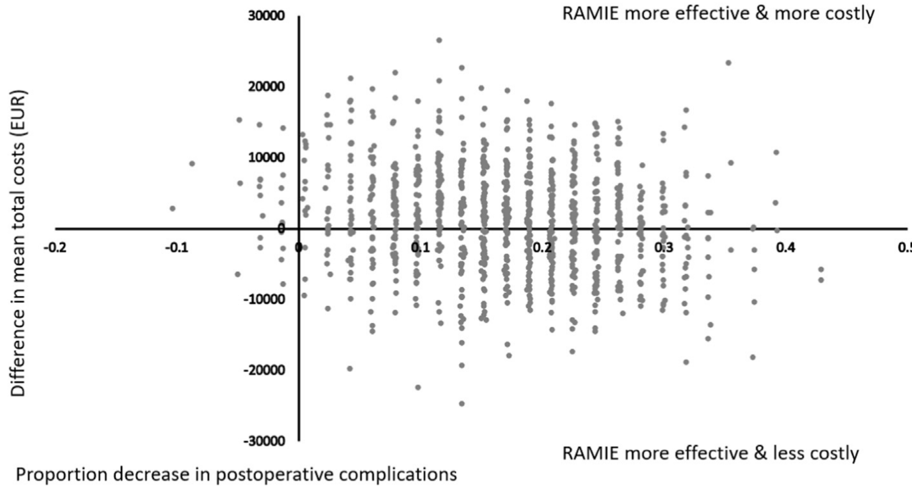

Fig. 2. Cost-effectiveness plane showing differences in total hospital costs (vertical axis) and difference in proportion of patients without postoperative complications (horizontal axis) between RAMIE and OTE. There are four possible outcomes: RAMIE is more costly and more effective: 55.4% (upper right quadrant), more costly and less effective: 1.6% (upper left), cheaper and less effective: 0.7%(lower left), or cheaper and more effective: 42.3% (lower right).

left quadrant). In 0.7%, RAMIE was cheaper, but resulted in more postoperative complications, whereas in 1.6% it was more expensive and resulted in more postoperative complications. Fig. 3 demonstrates the probability of RAMIE being cost-effective for different values of societal willingness to pay per complication prevented; at a willingness-to-pay threshold of €0, the probability was 42%, and at €10.000, €20.000, €25.000 and €40.000 it was 53%, 62%, 70% and 82%, respectively.

5.4. Risk factors associated with increased hospital costs in the entire cohort

An analysis of postoperative hospital costs for patient and treatment related characteristics, and postoperative complications after esophagectomy was performed in the entire cohort including all 109 patients who underwent a surgical procedure after randomization. Results are shown in Table 3. Factors associated with additional costs in univariable analysis included age, >70, ASA score, any comorbidity and postoperative complications. Major postoperative complications was the only factor that remained independently associated with an increase in mean total hospital costs in multivariable analysis (attributable costs of €31839 per patient with major complications, BCaCI €18919 to 46516 $p = 0.009$).

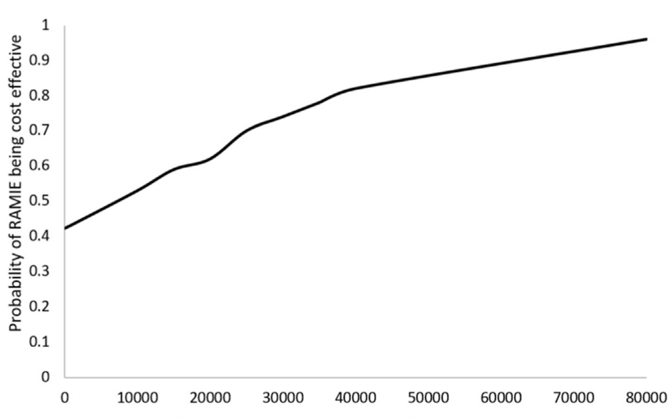

Fig. 3. Cost-effectiveness acceptability curve showing the probability of RAMIE being cost-effective for different values of willingness to pay per complication prevented.

6. Discussion

In the ROBOT-trial, total hospital costs were comparable between RAMIE and OTE. A postoperative complicated course was found to be the most important driver of hospital costs. Although the costs of the initial surgical procedure in the RAMIE group were higher, the comparable total hospital costs (costs of initial procedure combined with postoperative care) were caused by the lower complication rate in the RAMIE group. At a willingness-to-pay threshold of €20.000 to €25.000 (i.e. estimated additional costs to the hospital to treat patients with a complication) RAMIE had a probability 62%–70% of being cost effective to prevent postoperative complications.

To enable interpretation of the cost-effectiveness probabilities, information regarding the willingness-to-pay threshold for complication reduction is needed. The investment by a hospital to fund a new treatment can be considered worthwhile if the improvement in clinical outcome is valued enough to pay for it. Whereas the willingness-to-pay thresholds for QALY improvements is well established in available literature, no opinion has been published regarding what can be considered a reasonable amount to spend on complication prevention after esophagectomy by a hospital. According to two previously published studies from the Netherlands and Sweden, the average additional cost burden of any postoperative complicated course after esophagectomy ranged between €18500 and €22500 euro's [5,6]. In the current study, at willingness-to-pay thresholds of these amounts, RAMIE had a >60% probability of being cost effective to prevent postoperative complications. Indicating that for each complication prevented, RAMIE is likely to cost hospitals less than the costs to treat complications after surgery.

These results are in concordance with previously published results showing that minor and major postoperative complications are the main drivers of postoperative costs after esophagectomy [5,6]. In this context, several non-randomized studies have shown that the reduction in complications and faster postoperative recovery after conventional minimally invasive esophagectomy (MIE) compared to OTE outweigh the increased operative costs of MIE [10–13]. These results emphasize that the continuing adoption of minimally invasive surgical techniques to provide improved quality of care does not necessarily increase healthcare spending. However, in a time when healthcare resources are frequently constrained,

Table 3
For the entire cohort, analysis of postoperative hospital costs (in Euros) for patient, treatment related characteristics and postoperative complications after esophagectomy.

Characteristic	n (%)	Average costs	Difference in costs	P-value
Number of patients	109 (100)	39850 (32834, 48751)		
Gender (n (%))				
Male	88 (81)	36884 (30465, 44998)	−15939 (−46884, 6424)	0.239
Female	21 (19)	52278 (34178, 76750)		
Age at the time of Surgery				
<70 years	76 (70)	33239 (28797, 38981)	−21837 (−47113, −3313)	0.062
>70 years	33 (30)	55077 (37128, 77607)		
ASA Score				
I	24	29983 (24031, 37903)	−12653 (−24312, −996)	0.049
II-III	85	42636 (34533, 52136)		
Surgical procedure				
OTE	55	39495 (30611, 52032)	−715 (−14831, 14783)	0.932
RAMIE	54	40211 (32001, 51580)		
Any comorbidity				
No	25	30327 (24068, 38242)	'-12356 (−24230, −852)	0.042
Yes	84	42684 (34515, 52640)		
Neoadjuvant treatment				
No	13	42314 (21537, 77083)	2797 (−20346, 38720)	0.865
Yes	96	39516 (33316, 47241)		
Complications				
No complications	19	22620 (18455, 26753)		<0.001
Minor complications (MCDC 1−2)	50	31258 (25840, 37886)	−8637 (−17093, −1357)	
Major Complications (MCDC 3−5)	40	58774 (44187, 74981)	−36153 (−56996, −18363)	

Values are mean (95% bias-corrected and accelerated confidence intervals) costs estimated by non-parametric bootstrapping.

identification of strategies to reduce surgical costs should be considered relevant. For example, in the ROBOT trial, the thoracic phase of RAMIE was performed robotically and the abdominal phase was performed with conventional laparoscopy. For the abdominal phase, a full set of laparoscopic trocars, instruments and a harmonic ace were used. Currently, both phases of the operation are performed robotically and this reduces operative costs by re-using the robotic instruments used in the thoracic phase and saving the costs associated with an additional set of laparoscopic instruments.

The question remains whether RAMIE is superior to MIE considering postoperative outcomes and postoperative costs. MIE showed comparable short-term postoperative benefits compared to OTE in a randomized trial (TIME trial) [14]. Early results of the first randomized controlled trial comparing RAMIE with MIE for treatment of esophageal squamous cell carcinoma demonstrated, shorter duration of surgery, comparable complication rates and improved lymph node yield for the RAMIE group. So far no costs analysis was conducted [15]. Currently, there are two other multicenter randomized controlled trials recruiting patients comparing RAMIE to conventional MIE: the REVATE trial (ClinicalTrials.gov Identifier: NCT03713749) [16]· recruiting patients with esophageal squamous cell carcinoma and the ROBOT-2 trial (ClinicalTrials.gov Identifier: NCT04306458) recruiting patients with esophageal adenocarcinoma [17]. Postoperative costs will be an important secondary endpoint in these studies and will answer the question whether there is a difference in postoperative costs and cost-effectiveness between RAMIE and MIE.

Another important driver of costs after esophagectomy is the preoperative individual physical state (i.e. comorbidity) of the patient, as is demonstrated by the current study (Table 1) and previously published studies [5,18]. As most of these characteristics are well known risk-factors for postoperative complications, they are therewith also important direct drivers of postoperative costs [5]. There is increase in evidence that shows that prehabilitation before major (abdominal) surgery, by preoperative exercise programs and nutritional optimization, improves postoperative recovery and can reduce postoperative complications [19]. This suggests that investing in the optimization of the preoperative physical state of patients could not only improve of quality of care, but may also decrease postoperative costs.

Strengths of this study include the randomized design. Furthermore, the financial data used in this study represent the actual patient-specific costs of postoperative hospitalization using TD-ABC methodology, which results in a detailed overview of costs for every aspect of a patient's postoperative hospitalization [9]. Limitations of this study include the limited number of included patients in this single center randomized controlled trial, which was not powered to show a difference in postoperative costs. Also healthcare costs may vary between hospitals and different medical systems and therewith potentially influence the generalizability of the current results. As such, direct extrapolation of these results to other settings should be carefully considered. To handle the fundamental heterogeneity in hospital costs, as indicated by the wide BCaCI, and reduced statistical power bootstrapping was applied. In this technique the original trial's hospital costs and clinical outcome are run through a mathematical model to simulate hypothetical results, as if the same trial was conducted thousands of times over. These simulated cost-effectiveness ratios better represent the wide range of possible cost-effectiveness outcomes that could be expected in the population and is considered essential in estimating cost-effectiveness within randomised controlled trials [20]. Furthermore, the cost-analysis was restricted to a hospital perspective up to 90 days postoperatively. No information was gathered from a patient perspective (i.e. earlier return to work) and no data regarding costs was acquired beyond 90 days postoperatively.

In conclusion, RAMIE is an effective treatment that reduces the incidence of postoperative complications compared to open surgery without increasing total hospital costs.

CRediT authorship contribution statement

Lucas Goense: Study concepts, Study design, Data acquisition, Quality control of, Data curation, and algorithms, Data analysis and interpretation, Statistical analysis, Manuscript preparation, Manuscript editing, Manuscript review. **Pieter C. van der Sluis:** Study concepts, Study design, Data acquisition, Quality control of, Data curation, and algorithms, Data analysis and interpretation, Manuscript preparation, Manuscript editing, Manuscript review. **Sylvia van der Horst:** Study concepts, Study design, Data acquisition, Quality control of, Data curation, and algorithms, Data analysis and interpretation, Manuscript preparation, Manuscript editing, Manuscript review. **Evangelos Tagkalos:** Study concepts, Data analysis and interpretation, Manuscript preparation, Manuscript editing, Manuscript review. **Peter P. Grimminger:** Study concepts, Data analysis and interpretation, Manuscript preparation, Manuscript editing, Manuscript review. **Wouter van Dijk:** Study concepts, Quality control of, Data curation, and algorithms, Data analysis and interpretation, Manuscript preparation, Manuscript editing, Manuscript review. **Jelle P. Ruurda:** Study concepts, Study design, Data acquisition, Data analysis and interpretation, Manuscript preparation, Manuscript editing, Manuscript review. **Richard van Hillegersberg:** Study concepts, Study design, Data acquisition, Data analysis and interpretation, Manuscript preparation, Manuscript editing, Manuscript review.

References

[1] van der Sluis PC, Ruurda JP, van der Horst S, et al. Robot-assisted minimally invasive thoraco-laparoscopic oesophagectomy versus open transthoracic oesophagectomy for resectable oesophageal cancer, a randomized controlled trial (ROBOT trial). Trials 2012;13:230.
[2] van der Sluis PC, van der Horst S, May AM, et al. Robot-assisted minimally invasive thoracolaparoscopic oesophagectomy versus open transthoracic oesophagectomy for resectable oesophageal cancer: a randomized controlled trial. Ann Surg 2019;269:621–30.
[3] Sjoquist KM, Burmeister BH, Smithers BM, et al. Survival after neoadjuvant chemotherapy or chemoradiotherapy for resectable ooesophageal carcinoma: an updated meta-analysis. Lancet Oncol 2011;12:681–92.
[4] Barbash GI, Glied SA. New technology and health care costs–the case of robot-assisted surgery. N Engl J Med 2010;363:701–4.
[5] Goense L, van Dijk WA, Govaert JA, van Rossum PS, Ruurda JP, van Hillegersberg R. Hospital costs of complications after oesophagectomy for cancer. Eur J Surg Oncol. 201;43:696-702.
[6] Löfgren A, Åkesson O, Johansson J, Persson J. Hospital costs and health-related quality of life from complications after esophagectomy. Eur J Surg Oncol 2021 May;47(5):1042–7.
[7] Dindo D, Demartines N, Clavien P. Classification of surgical complications a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205–13.
[8] Kaplan RS, Anderson SR. Time-driven activity-based costing. Harv Bus Rev 2004;82. 131,138, 150.
[9] Barber JA, Thompson SG. Analysis of cost data in randomized trials: an application of the non-parametric bootstrap. Stat Med 2000 Dec 15;19(23):3219–36.
[10] Chao YK, Wen YW. Cost-effectiveness analysis of thoracoscopic versus open esophagectomy for esophageal cancer: a population-based study. Dis Esophagus 2021 Aug 10;34(8):doaa116.
[11] Liu CY, Lin CS, Shih CS, Huang YA, Liu CC, Cheng CT. Cost-effectiveness of minimally invasive esophagectomy for esophageal squamous cell carcinoma. World J Surg 2018 Aug;42(8):2522–9.
[12] Lee L, Sudarshan M, Li C, Latimer E, Fried GM, Mulder DS, et al. Cost-effectiveness of minimally invasive versus open esophagectomy for esophageal cancer. Ann Surg Oncol 2013 Nov;20(12):3732–9. https://doi.org/10.1245/s10434-013-3103-6.
[13] Fu SJ, Ho VP, Ginsberg J, Perry Y, Delaney CP, Linden PA, et al. Complications, not minimally invasive surgical technique, are associated with increased cost after esophagectomy. Minim Invasive Surg 2016;2016:7690632.
[14] Biere SS, Van Berge Henegouwen MI, Maas KW, et al. Minimally invasive versus open ooesophagectomy for patients with ooesophageal cancer: a multicentre open-label, randomised controlled trial. Lancet 2012;379:1887–92.
[15] Yang Y, Li B, Yi J, et al. Robot-assisted versus conventional minimally invasive oesophagectomy for resectable oesophageal squamous cell carcinoma: early results of a multicenter randomized controlled trial: the RAMIE trial. Ann Surg 2021. Apr 1;275(1):646–53.
[16] Chao YK, Li ZG, Wen YW, Kim DJ, Park SY, Chang YL, et al. Robotic-assisted Oesophagectomy vs Video-Assisted Thoracoscopic Oesophagectomy (REVATE): study protocol for a randomized controlled trial. Trials 2019;20:346.
[17] Tagkalos E, van der Sluis PC, Berlth F, et al. Robot-assisted minimally invasive thoraco-laparoscopic oesophagectomy versus minimally invasive oesophagectomy for resectable oesophageal adenocarcinoma, a randomized controlled trial (ROBOT-2 trial). BMC Cancer 2021 Sep 26;21(1):1060.
[18] Liu Q, Yu YK, Wang DY, Xing WQ. Factors associated with the costs of hospitalization after esophagectomy: a retrospective observational study at a three-tertiary cancer hospital in China. J Thorac Dis 2020 Oct;12(10):5970–9.
[19] Doganay E, Moorthy K. Prehabilitation for esophagectomy. J Thorac Dis 2019 Apr;11(Suppl 5):S632–8.
[20] Angevine PD, Berven S. Health economic studies: an introduction to cost-benefit, cost-effectiveness, and cost-utility analyses. Spine 2014 Oct 15;39(22 Suppl 1):S9–15.