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ORIGINAL CONTRIBUTION

Transanal Total Mesorectal Excision Versus Anterior Total Mesorectal Excision For Rectal Cancer: A Propensity-Score Matched, Population-Based Study In Catalonia, Spain

Short running head: TaTME VS ANTERIOR TME FOR RECTAL CANCER

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ABSTRACT

BACKGROUND: The clinical value of transanal total mesorectal excision is debated.

OBJECTIVE: To compare short- and medium-term effects of transanal versus anterior total mesorectal excision for rectal cancer.

DESIGN: This was a multicenter retrospective cohort study.

SETTING: The study included all Catalonian public hospitals.

PATIENTS: All non-metastatic patients receiving transanal or anterior total mesorectal excision (open or laparoscopic) for primary rectal cancer in 2015-16.

MAIN OUTCOME MEASURES: Data on vital status were collected to March 2019. Between-group differences were minimized by applying propensity score matching to baseline patient characteristics. Competing risk models were used to assess systemic and local recurrence along with death at two years, and multivariable Cox regression to assess two-year disease-free survival. Results are expressed with their 95% confidence intervals.

RESULTS: The final subsample was 537 patients receiving total mesorectal excision (transanal approach: n=145; anterior approach: n=392). Median follow-up was 39.2 months (interquartile range 33.0-45.8). Accounting for death as a competing event, there was no association between transanal total mesorectal excision and local recurrence (matched sub-hazard ratio 1.28, 0.55–2.96). There were no statistical differences in the comparative rate of local recurrence (transanal: 1.77 per 100 person-years, 0.76–3.34; anterior: 1.37 per 100 person-year, 0.8–2.15) or mortality (transanal: 3.98 per 100 person-year, 2.36–6.16; anterior: 2.99 per 100 person-years, 2.1-4.07). Groups presented similar two-year cumulative incidence of local recurrence (4.83% versus 3.57%, respectively) and disease-free survival (hazard ratio 1.33, 0.92–1.92).

LIMITATIONS: We used data only from the public system, the study is retrospective, and data on individual surgeons are not reported.

CONCLUSION: These population-based results support the use of either the transanal, open, or laparoscopic approach for rectal cancer in Catalonia. See **Video Abstract** at http://links.lww.com/DCR/Bxxx.

ESCISIÓN MESORRECTAL TOTAL TRANSANAL VERSUS ESCISIÓN MESORRECTAL TOTAL ANTERIOR PARA EL CÁNCER DE RECTO: UN ESTUDIO POBLACIONAL CON EMPAREJAMIENTO DE PUNTAJE DE PROPENSIÓN EN CATALUÑA, ESPAÑA

ANTECEDENTES: Se debate el valor clínico de la escisión mesorrectal total transanal.

OBJETIVO: Comparar los efectos a corto y mediano plazo de la escisión mesorrectal total transanal versus anterior para el cáncer de recto.

DISEÑO: Este fue un estudio de cohorte retrospectivo multicéntrico.

AJUSTE: El estudio incluyó a todos los hospitales públicos de Cataluña.

PACIENTES: Todos los pacientes no metastásicos que recibieron escisión mesorrectal total anterior o transanal (abierta o laparoscópica) por cáncer de recto primario en 2015-16.

PRINCIPALES MEDIDAS DE VALORACION: Los datos sobre el estado vital se recopilaron hasta marzo de 2019. Las diferencias entre los grupos se minimizaron aplicando el emparejamiento de puntajes de propensión a las características iniciales del paciente. Se utilizaron modelos de riesgo en competencia para evaluar la recurrencia sistémica y local junto con la muerte a los dos años, y la regresión de Cox multivariable para evaluar la supervivencia libre de enfermedad a dos años. Los resultados se expresan con sus intervalos de confianza del 95%.

RESULTADOS: La submuestra final fue de 537 pacientes que recibieron escisión mesorrectal total (abordaje transanal: n = 145; abordaje anterior: n = 392). La mediana de seguimiento fue de 39,2 meses (rango intercuartílico 33,0-45,8). Teniendo en cuenta la muerte como un evento competitivo, no hubo asociación entre la escisión mesorrectal total transanal y la recurrencia local (cociente de sub-riesgo apareado 1,28, 0,55-2,96). No hubo diferencias estadísticas en la tasa comparativa de recurrencia local (transanal: 1,77 por 100 personas-año, 0,76-3,34; anterior: 1,37 por 100 personas-año, 0,8-2,15) o mortalidad (transanal: 3,98 por 100 personas-año, 2,36–6,16; anterior: 2,99 por 100 personas-año, 2,1-4,07). Los grupos presentaron una incidencia acumulada de dos años similar de recidiva local (4,83% frente a 3,57%, respectivamente) y supervivencia libre de enfermedad (índice de riesgo 1,33, 0,92–1,92).

LIMITACIONES: Utilizamos datos solo del sistema público, el estudio es retrospectivo y no se informan datos sobre cirujanos individuales.

CONCLUSIÓN: Estos resultados basados en la población apoyan el uso del abordaje transanal, abierto o laparoscópico para el cáncer de recto en Cataluña. Consulte. **Video Resumen** en http://links.lww.com/DCR/Bxxx. *(Traducción— Dr. Francisco M. Abarca-Rendon)*

KEY WORDS: Mesorectal excision; Population-based; Propensity-score matching analysis; Rectal cancer; Surgery; Transanal mesorectal excision.

INTRODUCTION

The centralization of complex cancer surgery in Catalonia, starting in 2011, has been accompanied by periodic external audits by the Catalan Cancer Plan to monitor quality and outcomes.[1] In rectal cancer, the audits have been instrumental in showing the benefits of the centralization policy for both the quality of the cancer treatment process and clinical outcomes.[2,3]

Our most recent audit included all patients who underwent surgery in 2015-2016, a period marked by the introduction of a new surgical procedure, transanal total mesorectal excision (TaTME). TaTME, which was first performed in Catalonia in 2009, is said to improve resection quality, especially in obese, male patients, with narrow pelvis and mid-low tumours.[4,5] However, this procedure can be technically challenging, and formal research and structured training are encouraged for safe implementation. Otherwise, patient experience and safety may be compromised, as we have seen with concerns such as an increased risk of urethral injuries.[6] The most serious international

debate revolves around its oncological safety with the Norwegian Colorectal Cancer Group reporting an unexpected pattern of early recurrences following TaTME.[7,8] Pending a national audit, the country declared a moratorium on the procedure.[9] Given this uncertainty, we decided to analyze the outcomes in Catalonia, studying both recurrence and survival to assess the oncological safety and effectiveness of TaTME from a public health perspective. The aim of this study was to compare TaTME versus anterior total mesorectal excision (TME) for surgical treatment of rectal cancer.

METHODS

Study design and population

This multicenter retrospective cohort study included all patients with rectal adenocarcinoma who had surgery with curative intent in the Catalan public healthcare system in 2015 and 2016 and were followed to March 2019. The healthcare system is based on a National Health Service model with universal access. Private hospitals were not included in the audits, so the 10% of patients in Catalonia who underwent surgery for rectal cancer outside the public healthcare system were not included. Surgeons performing TaTME were either pioneers of the technique or had undergone a structured training programme.[10]

We restricted our comparative analysis to patients with stages I–III cancer, with tumours up to 13 cm from the anal verge who underwent surgical excision with TaTME or (open or laparoscopic) anterior TME. We excluded patients who underwent abdominoperineal excision, Hartmann's procedure, or transanal local excision; those with premalignant lesions and synchronous metastases, detected at diagnosis or intraoperatively; and patients receiving emergency or palliative therapy.

Outcomes and data collection

Primary endpoints were local and systemic recurrence, and disease-free and overall survival. Secondary endpoints were overall morbidity and anastomotic leakage (any pelvic abscess was considered anastomotic leakage). We determined follow-up time, local recurrence (LR), systemic recurrence and death based on the date of the primary rectal surgery. By linking the study database with the Catalan registry of insured persons, we were able to collect data on the vital status of all patients to March 2019. Cause of death was unknown due to confidentiality issues. We defined LR as any histologically or image-confirmed tumor present within the pelvis, whether alone or with distant metastases; and systemic recurrence as expansion of the tumor beyond the surgical field to other organs like the liver, lung or bones. Trained external auditors identified cases and retrieved data from the health information system. Data were collected and standardized using a purpose-designed form, accompanied by clear instructions and pertinent definitions; both instruments had been previously validated.[1,3] Postoperative complications were graded according to the Clavien-Dindo classification.[11] Follow-up was defined as "surgery to date of death or last entry on the medical chart".

An external visiting surgeon (FP) trained the auditors to collect data on postsurgical complications and performed quality control by directly supervising a random sample of 277 cases.

The Clinical Research Ethics Committee of Bellvitge University Hospital approved the study protocol.

After early postsurgical follow-up, visits were scheduled every three months for the first two years and every six months for three years thereafter. Each visit included anamnesis, physical evaluation, digital rectal examination and/or proctoscopy and blood test with carcinoembryonic antigen. Imaging studies (thoracic and abdominopelvic CT scan) were performed every six months for the first two years and annually for the remaining three years. One year after surgery, a complete colonoscopy was performed.[12] Suspected LR prompted pelvic magnetic resonance imaging and/or transrectal ultrasound-guided needle biopsy.

Statistical analysis

Categorical variables are presented as absolute and relative frequencies; associations between them were analyzed using Pearson's χ^2 or Fisher's exact test, as appropriate. Continuous variables are presented as the median and interquartile range (IQR) and compared using the student's t-test or the Mann-Whitney U test.

Propensity score matching (PSM) was carried out to minimize the differences between the TaTME and anterior TME group. This statistical technique uses the patient's clinical characteristics to estimate the probability that they will be in the anterior TME group. For each patient receiving TaTME, the nearest neighbor matching algorithm was used to select three patients from the anterior TME group, with a maximum tolerance distance between the matched subjects of 0.1 standard deviations.[13]

Confounding variables used to compute the propensity score were gender, age, American Society of Anesthesiologists (ASA) score, distance from anal verge, neoadjuvant treatment, pT and pN. The cohort of patients matched by surgical approach was used for the remaining analysis. Competing risk analyses were also performed considering the different outcomes and the time to recurrence (local and/or systemic) and death. Because presence of one of these factors precludes or modifies the probability of the others, we modelled the risk of each event using competing risk proportional hazards models.[14]

We report the event rate per 100 person-years follow-up, cumulative incidences, and the sub-hazard ratio (sHR) with its 95% confidence interval (CI), obtained from competing risk models.

Time until death was assessed using the Kaplan–Meier estimator. The log-rank test was used to compare the risk of LR and mortality between study groups. Cox regressions were used for survival analyses, which are reported with HRs and 95% CIs. We used the Schoenfeld residuals to verify the proportionality of hazards in the Cox model.

Similarly to the Norwegian Colorectal Cancer Group study, we created a cohort of stage I–III patients who survived to three months post-surgery. After PSM, survival analyses were performed as described elsewhere.[7]

Two-sided p values of less than 0.05 were considered statistically significant. The R statistical package (version 3.6.1, cran.r-project.org) was used for statistical analyses.

We used the STROBE cohort checklist when writing our report.[15]

RESULTS

The audit identified 1879 patients with rectal cancer who were operated on with a curative intent during the study period. While 12 centers performed TaTME, 60% of these procedures took place in two hospitals, while the other 10 centers each performed

less than 10% of the total (See bar graph in supplementary materials). Several centers carried out just one or two procedures in the last year of the audit. After applying inclusion and exclusion criteria, 934 patients were included (Figure 1).

Table 1 shows the baseline characteristics of those patients (TaTME n=145 vs anterior TME n=789). A slightly lower proportion of TaTME patients had level III ASA physical status. This group also presented a shorter distance to anal verge, lower abdominal conversion, and a significantly lower percentage of adjuvant treatment. Anastomotic leakage and pelvic abscess were also reported in a slightly lower proportion of patients in the TaTME group (p=0.537).

The PSM (1:3) in these 934 patients resulted in a final matched sample of 537 patients. Table 2 presents the post-matching distribution of key variables. Supplementary data outline the reduction of standardized mean differences between groups after PSM, making the two groups comparable on matching variables. After PSM, the rate of abdominal conversion remained lower in the TaTME group, while the percentage of anastomotic leakage was similar (p=0.619). The proportion receiving adjuvant therapy was 20% lower in the TaTME group (54.1% vs 35.2%; p<0.01). No statistical differences were detected in the proportion of positive distal margin results between the two groups (anterior TME group, 2.1%; TaTME group, 0.8%; p=0.359). Regarding the circumferential resection margin (CRM), there was a slightly higher proportion of positive margins in the TaTME group than in the anterior TME group (5.5% vs. 1.8%, p=0.053). Regarding R1 resection, there was also a higher proportion in the TaTME group (6.2% vs. 2.6%), although the difference was not statistically significant (p=0.102). Although there were no statistical differences between groups in the quality of mesorectal excision, the proportion of complete mesorectum was higher in the TaTME group (86.9% vs 80.6%).

Median follow-up for the overall sample was 38.9 (IQR 33.0-45.3) months, during which there were no statistical differences in LR and death rates by surgical approach. LR incidence was 1.77 per 100 person-years (95% CI 0.76–3.34) in the TaTME group and 1.37 per 100 person-years (95% CI 0.8–2.15) in the anterior TME group. The mortality rates were 3.98 per 100 person-years (95% CI 2.36–6.16) and 2.99 per 100 person-years (95% CI 2.1–4.07), respectively, while the two-year cumulative incidence of LR was 4.83% and 3.57%, respectively (table 3). Accounting for death as a competing event, there was no association between TaTME and LR hazard (matched sHR 1.28; 95% CI 0.55–2.96; Fig 2).

We assessed the probability of both local and systemic recurrence along with death under a competing risk analysis. In the TaTME and anterior TME groups, respective rates were: for LR incidence, 1.73 per 100 person-years (95% CI 0.7–3.4) and 1.48 per 100 person-years (95% CI 0.86–2.31); mortality, 2.22 per 100 person-years (95% CI 1.02–4.06) and 2.0 per 100 person-years (95% CI 1.27–2.94); and systemic recurrence, 6.18 per 100 person-years (95% CI 4.0–8.97) and 4.17 per 100 person-years (95% CI 3.07–5.48). Accounting for death and systemic recurrence as competing events, there was no statistical association between TaTME and LR hazard (matched adjusted sHR 1.11; 95% CI 0.46–2.68; Fig. 3). There were no differences in the risk of systemic recurrence (matched sHR 1.45; 95% CI 0.89 to 2.36; Fig. 3) or disease-free survival (HR 1.33; 95% CI 0.92–1.92; Fig. 4). Table 4 shows the two-year cumulative incidence of local and systemic recurrence and mortality. The 95% confidence intervals of the cumulative incidence of LR, systemic recurrence and mortality each one at 3 months, 1

and 2 years in the TaTME and the Anterior TME group overlap, indicating that there is no statistical difference between both surgical techniques for these clinical outcomes.

In the cohort we created based on the Norwegian study, the association between TaTME and LR hazard or TaTME and mortality hazard was statistically non-significant (matched adjusted LR HR 0.92; 95% CI 0.37–2.26; matched adjusted mortality HR 0.94; 95% CI 0.54–1.63).

Finally, in the TaTME group, the most common sites of LR were presacral (n=4) and anterior (n=2), whereas in the anterior TME group they were the presacral space (n=5) and the anastomotic stump (n=5). There was a single case of multifocal LR growth with two sites in the TaTME group and none in the anterior TME group (Supplementary material).

DISCUSSION

This study describes the short- and medium-term clinical outcomes of TaTME versus anterior TME for rectal cancer surgery in a large population-based cohort in Catalonia. We found no statistically significant differences in recurrence or survival between groups, which is very relevant considering the publication of disturbing reports published elsewhere showing higher rates and new patterns of recurrence after TaTME.[7,16]

The Norwegian Colorectal Cancer Group first reported the results of 110 TaTME procedures performed from January 2015 to December 2017, primarily in 4 of the 20 hospitals where surgery for primary rectal cancer is centralized. Authors observed an unexpectedly higher rate of early LR in patients receiving TaTME (9.4%) compared with TME (3.4%). In some cases, LR showed rapid, multifocal growth in the pelvic cavity and sidewalls, different from that typically observed after conventional surgery. These results led to a national moratorium on TaTME pending a national audit of clinical outcomes.[9] When completed, the results confirmed the high LR rate: 7.9% of all 152 patients who had undergone TaTME.[7]

In the Netherlands, another study reported oncological outcomes in the first 10 patients treated with TaTME in each of 12 centers participating in a structured training pathway.[16] Despite a low positive CRM rate, overall LR was 10% (12/120), with a mean interval to recurrence of 15 months. Moreover, multifocal LR was also present in 8 of the 12 patients. Authors suggested that these unfavourable oncological results may result from a lack of experience during the initial phase of the learning curve.

Other authors have also assessed oncological outcomes after TaTME reporting however good locoregional control.[8,17,18] Hol et al. analysed 159 consecutive patients undergoing TaTME for mid- or low rectal cancer in two referral centers in the Netherlands between January 2012 and April 2016.[18] At three and five years, the LR rate was 2.0% and 4.0%, while disease-free survival was 92% and 81%. The authors concluded that TaTME is oncologically safe, but further robust and audited data were needed to confirm the findings. An international observational cohort study in six tertiary referral centres included 767 consecutive TaTME cases for mid- and low rectal cancer. After a median of 25.5 months, 24 patients developed LR, with an actuarial cumulative two-year LR rate of 3%. No multifocal LR pattern was observed.[8] Finally, a single-center retrospective study in Denmark included 200 patients receiving TaTME from December 2013 to July 2019. LR occurred in 4.7% of the patients followed for at least two years; overall survival was 90% and disease-free survival, 81%.[17]

These three studies lacked a concurrent control group, which substantially limits the evaluation of intervention effects in a binary analysis.[8,17,18] Moreover, they took place in a single center or in a few highly selected institutions. In contrast, our study data came from a large population-based cohort. Although the study excluded private centers, the public healthcare system in Spain provides care for nearly 90% of patients receiving rectal cancer surgery in Catalonia; thus, our study had high coverage and was representative of the population. One study limitation is its retrospective nature; to minimize potential inaccuracies in data collection, we employed a trained team of professionals and purpose-designed instruments. In addition, our team presented individual hospital results to the respective centers, which yielded feedback used in the validation of results.

Another strength of our study is the comparison of TaTME with a control group of patients undergoing anterior TME, by means of PSM. This method reduces the selection bias by matching the sample for selected variables. Nevertheless, some residual selection bias may exist for other variables. All variables we used in the matching are critical for defining the patients' prognosis, and adjustment for confounders was effective (see supplemental figure). The main limitation from this perspective is the lack of data on body mass index, since this variable was not included in the clinical audit. In addition to PSM, competitive risk analysis was applied to adjust for the mutual interaction between local and systemic recurrence and death, as the presence of any of these variables modifies or (in the case of death) precludes the probability of the others occurring. We did not collect data on surgeons performing each procedure because the audit was for the hospital multidisciplinary team rather than specific to each professional involved.

The TaTME technique was introduced by one pioneer hospital, while a second was an early adopter. At the time of the audit, 60% of TaTME took place in these two hospitals, the other 10 centers each performed less than 10% of the total. This distribution is indicative of a preliminary stage in the dissemination of this surgical innovation.

Some aspects deserve careful analysis. Firstly, the higher proportion of positive CRM in the TaTME group compared to the anterior TME group was not statistically significant ($p=0.053$). Regarding the higher R1 resection proportion in the TaTME group was either not statistically significant ($p=0.102$). And the overall LR rates, of less than 5%, meet quality standards for the surgical excision of rectal cancer.

Moreover, we found just one case of LR with a multifocal pattern. Although the median follow-up was about 39 months, this is the period when most recurrences are detected.[19]

Furthermore, the results in both groups are consistent with the findings of one meta-analysis as well as other published retrospective analyses.[8,17,18,20] Although not statistically different, the TaTME cohort did show a slightly higher risk of systemic recurrence, which could be at least partially explained by the lower proportion of patients receiving adjuvant treatment. In turn, the difference in adjuvant treatment could be explained by a lower prevalence of pathological stage III. These data may have given medical oncologists an overall impression of lower risk of recurrence.

Finally, there were no significant differences in the rates of anastomotic leakage between the two groups. This is of special note considering that during the study period, implementation of TaTME was in an early stage in Catalonia, which can be associated with higher morbidity. In contrast, the rates of anastomotic leakage and pelvic abscess reported in some recent studies have been around 15% to 20%.[16,18] Furthermore, the patients who underwent TaTME in our study showed significantly lower conversion

compared to those receiving anterior TME. This finding is of interest, since a lower conversion risk is one of the possible benefits initially attributed to TaTME, and converted cases may be at greater risk than unconverted laparoscopy for some unfavorable short-term outcomes.[21,22] To confirm this potential advantage of TaTME in Catalonia, it will be necessary to analyze a larger cohort once the implementation phase has been completed.

CONCLUSION

To conclude, the research question driving this paper was whether TaTME was safe compared with anterior TME from an oncological perspective. Our results show similar and satisfactory medium-term oncological outcomes between TaTME and anterior TME. Therefore, until completion of ongoing randomized controlled trials, these data support the use of either the transanal, open, or laparoscopic approach for rectal cancer in Catalonia.[23,24]

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FIGURE LEGENDS

Figure 1. Flow chart showing selection of study participants.

Figure 2. Cumulative incidence of mortality and local recurrence by surgical approach. Footnotes: M: Mortality; LR: local recurrence.

Figure 3. Cumulative incidence of mortality, local recurrence and systemic recurrence by surgical approach. Footnotes: M: Mortality; LR: local recurrence; S: systemic recurrence.

Figure 4. Disease-free survival by surgical procedure.

Table 1. Baseline characteristics of cohort

Variables	Total	Anterior TME	Transanal TME	p
N	934	789	145	
Age, years				0.611
Median (IQR)	68.2 (59.5;75.4)	68.0 (59.5;75.3)	68.7 (59.6;75.5)	
Women, N (%)	307 (32.9%)	262 (33.2%)	45 (31.0%)	0.609
ASA scale, N (%)				0.051
ASA I	40 (4.3%)	34 (4.3%)	6 (4.1%)	
ASA II	564 (60.4%)	464 (58.8%)	100 (69.0%)	
ASA III	314 (33.6%)	279 (35.4%)	35 (24.1%)	
ASA IV	16 (1.7%)	12 (1.5%)	4 (2.8%)	
TNM staging, N (%)				0.509
0/I	145 (15.5%)	119 (15.1%)	26 (17.9%)	
II	190 (20.3%)	158 (20.0%)	32 (22.1%)	
III	599 (64.1%)	512 (64.9%)	87 (60.0%)	
Distance from anal verge				<0.001
Median (IQR)	9.0 (6.0;10.0)	10.0 (7.0;10.0)	8.0 (5.0;10.0)	
Location, N (%)				
Distal rectum (2-6 cm)	246 (26.3%)	189 (24.0%)	57 (39.3%)	
Middle rectum (7-11 cm)	530 (56.7%)	457 (57.9%)	73 (50.3%)	
Proximal rectum (12-13 cm)	158 (16.9%)	143 (18.1%)	15 (10.3%)	
pT, N (%)				0.306
pT0	132 (14.1%)	108 (13.7%)	24 (16.6%)	
pT1	76 (8.1%)	66 (8.4%)	10 (6.9%)	
pT2	257 (27.5%)	216 (27.4%)	41 (28.3%)	
pT3	411 (44.0%)	344 (43.6%)	67 (46.2%)	
pT4	40 (4.3%)	38 (4.8%)	2 (1.4%)	
pTis	18 (1.9%)	17 (2.2%)	1 (0.7%)	
pN, N (%)				0.576
pN0	643 (68.8%)	541 (68.6%)	102 (70.3%)	
pN1	205 (21.9%)	172 (21.8%)	33 (22.8%)	
pN2	86 (9.2%)	76 (9.6%)	10 (6.9%)	
Abdominal approach, N (%)				<0.001
Open surgery	159 (17.0%)	156 (19.8%)	3 (2.1%)	
Laparoscopy	775 (83.0%)	633 (80.2%)	142 (97.9%)	
Laparoscopy conversion[1]	81 (10.5%)	75 (11.8%)	6 (4.2%)	0.013
Neoadjuvant treatment, N (%)	647 (69.3%)	551 (69.8%)	96 (66.2%)	0.384
Adjuvant treatment, N (%)	485 (51.9%)	434 (55.0%)	51 (35.2%)	<0.001
Anastomotic leakage	138 (14.7%)	119 (15.1%)	19 (13.1%)	0.537
Lymph nodes examined				0.051
Median (IQR)	15.0 (10.0;20.0)	15.0 (10.0;21.0)	14.0 (10.5;17.0)	
Lymph nodes affected				0.437
Median (IQR)	0.0 (0.0;1.0)	0.0 (0.0;1.0)	0.0 (0.0;1.0)	
Circumferential margin				0.067
Negative	878 (94.0%)	745 (94.4%)	133 (91.7%)	

Positive	26 (2.8%)	18 (2.3%)	8 (5.5%)	
Not evaluable	19 (2.0%)	15 (1.9%)	4 (2.8%)	
Missing	11 (1.2%)	11 (1.4%)	0 (0.0%)	
Distal margin				0.388
Negative	905 (96.9%)	765 (97.0%)	140 (96.6%)	
Positive	12 (1.3%)	9 (1.1%)	3 (2.1%)	
Not evaluable	8 (0.9%)	6 (0.8%)	2 (1.4%)	
Missing	9 (1.0%)	9 (1.1%)	0 (0.0%)	
Radicality of resection[2]				0.188
R0	869 (93.0%)	737 (93.4%)	132 (91.0%)	
R1	34 (3.6%)	25 (3.2%)	9 (6.2%)	
Missing	31 (3.3%)	27 (3.4%)	4 (2.8%)	
Quality of mesorectal excision (pathology report)				0.095
No reported/missing	30 (3.2%)	28 (3.5%)	2 (1.4%)	
M[3]. complete	748 (80.1%)	622 (78.8%)	126 (86.9%)	
M. nearly complete	80 (8.6%)	72 (9.1%)	8 (5.5%)	
M. incomplete	53 (5.7%)	49 (6.2%)	4 (2.8%)	
Reported: missing	23 (2.5%)	18 (2.3%)	5 (3.4%)	
Follow-up (months)				0.987
Median (IQR)	38.9 (33.0;45.3)	38.9 (33.0;45.3)	39.0 (32.8;47.0)	

2-sided P values < 0.05 were considered to indicate statistical significance.

IQR: Interquartile range

Missing: no data found

1. Calculated on total of laparoscopic surgeries
2. Based on pathological results: R0 for negative CRM and negative DRM; R1 for Positive Circumferential margin and/or positive distal margin; Missing if both CRM and DRM are missing or one of the two is negative and the other is unknown).
3. Mesorectum

Follow-up: from surgery to last control or death

Table 2. Cohort characteristics after propensity score matching

Variables	Total	Anterior TME	Transanal TME	p
N	537	392	145	
Age*, years				0.391
Median (IQR)	67.9 (59.4;74.9)	67.4 (59.1;74.8)	68.7 (59.6;75.5)	
Women*, N (%)	173 (32.2%)	128 (32.7%)	45 (31.0%)	0.722
ASA scale*, N (%)				0.876
ASA I	26 (4.8%)	20 (5.1%)	6 (4.1%)	
ASA II	357 (66.5%)	257 (65.6%)	100 (69.0%)	
ASA III	140 (26.1%)	105 (26.8%)	35 (24.1%)	
ASA IV	14 (2.6%)	10 (2.6%)	4 (2.8%)	
Neoadjuvant treatment*, N (%)	372 (69.3%)	276 (70.4%)	96 (66.2%)	0.349
pT*, N (%)				0.992
pT0	88 (16.4%)	64 (16.3%)	24 (16.6%)	
pT1	41 (7.6%)	31 (7.9%)	10 (6.9%)	
pT2	156 (29.1%)	115 (29.3%)	41 (28.3%)	
pT3	241 (44.9%)	174 (44.4%)	67 (46.2%)	
pT4	6 (1.1%)	4 (1.0%)	2 (1.4%)	
pTis	5 (0.9%)	4 (1.0%)	1 (0.7%)	
pN*, N (%)				0.918
pN0	380 (70.8%)	278 (70.9%)	102 (70.3%)	
pN1	117 (21.8%)	84 (21.4%)	33 (22.8%)	
pN2	40 (7.4%)	30 (7.7%)	10 (6.9%)	
Distance from anal verge*				0.374
Median (IQR)	8.0 (5.0;10.0)	8.0 (5.0;10.0)	8.0 (5.0;10.0)	
TNM staging, N (%)				0.526
0/I	91 (16.9%)	65 (16.6%)	26 (17.9%)	
II	104 (19.4%)	72 (18.4%)	32 (22.1%)	
III	342 (63.7%)	255 (65.1%)	87 (60.0%)	
Location, N (%)				0.590
Distal rectum (2-6 cm)	193 (35.9%)	136 (34.7%)	57 (39.3%)	
Middle rectum (7-11 cm)	282 (52.5%)	209 (53.3%)	73 (50.3%)	
Proximal rectum (12-13 cm)	62 (11.5%)	47 (12.0%)	15 (10.3%)	
Abdominal approach, N (%)				<0.001
Open surgery	78 (14.5%)	75 (19.1%)	3 (2.1%)	
Laparoscopy	459 (85.5%)	317 (80.9%)	142 (97.9%)	
Laparoscopy conversion[1]	47 (10.2%)	41 (12.9%)	6 (4.2%)	0.008
Adjuvant treatment, N (%)	263 (49.0%)	212 (54.1%)	51 (35.2%)	<0.001
Anastomotic leakage	77 (14.3%)	58 (14.8%)	19 (13.1%)	0.619
Lymph nodes examined				0.296
Median (IQR)	14.0 (10.0;19.0)	14.0 (10.0;20.0)	14.0 (10.5;17.0)	
Lymph nodes affected				0.970
Median (IQR)	0.0 (0.0;1.0)	0.0 (0.0;1.0)	0.0 (0.0;1.0)	

Circumferential margin				0.053
Negative	503 (93.7%)	370 (94.4%)	133 (91.7%)	
Positive	15 (2.8%)	7 (1.8%)	8 (5.5%)	
Not evaluable	13 (2.4%)	9 (2.3%)	4 (2.8%)	
Missing	6 (1.1%)	6 (1.5%)	0 (0.0%)	
Distal margin				0.359
Negative	521 (97.0%)	381 (97.2%)	140 (96.6%)	
Positive	6 (1.1%)	3 (0.8%)	3 (2.1%)	
Not evaluable	6 (1.1%)	4 (1.0%)	2 (1.4%)	
Missing	4 (0.7%)	4 (1.0%)	0 (0.0%)	
Radicality of resection[2]				0.102
R0	498 (92.7%)	366 (93.4%)	132 (91.0%)	
R1	19 (3.5%)	10 (2.6%)	9 (6.2%)	
Missing	20 (3.7%)	16 (4.1%)	4 (2.8%)	
Quality of mesorectal excision (pathology report)				
Not reported	14 (2.6%)	12 (3.1%)	2 (1.4%)	
M[3]. complete	442 (82.3%)	316 (80.6%)	126 (86.9%)	
M. nearly complete	41 (7.6%)	33 (8.4%)	8 (5.5%)	
M. incomplete	27 (5.0%)	23 (5.9%)	4 (2.8%)	
Reported: missing	13 (2.4%)	8 (2.0%)	5 (3.4%)	
Follow-up (months)				0.779
Median (IQR)	39.2 (33.0;45.8)	39.4 (33.1;45.6)	39.0 (32.8;47.0)	

*. Variables matching
P values below 0.05 (two-sided) were considered to indicate statistical significance.
IQR: Interquartile range

Missing: no data found

1. Calculated on total of laparoscopic surgeries
2. Based on pathological results: R0 for negative CRM and negative DRM; R1 for Positive Circumferential margin and/ or positive distal margin; Missing if both CRM and DRM are missing or one of the two is negative and the other is unknown).
3. Mesorectum

Follow-up: from surgery to last control or death

Table 3. Cumulative incidence of local recurrence and mortality at 3 months, 1 and 2 years by surgical approach

Time from surgery	Anterior TME		TaTME	
	LR	Mortality	LR	Mortality
3 months	0	0.77 [0.21; 2.10]	0	1.38 [0.27; 4.49]
1 year	1.28 [0.49; 2.81]	3.06 [1.67; 5.13]	1.38 [0.27; 4.49]	2.76 [0.91; 6.45]
2 years	3.57 [2.05; 5.76]	5.87 [3.83; 8.50]	4.83 [2.13; 9.20]	6.21 [3.04; 10.95]

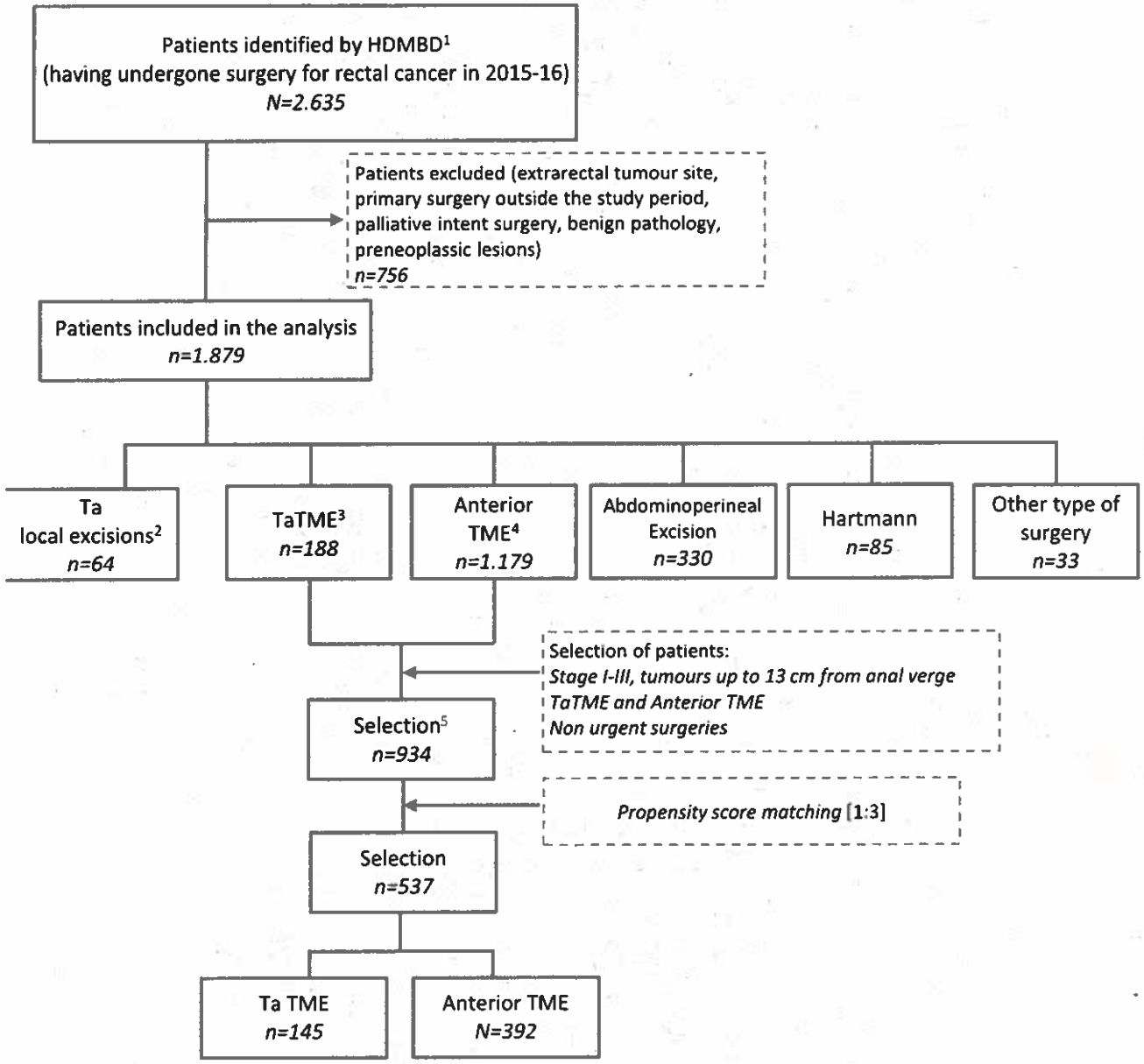
[95% Confidence Interval]

Table 4. Cumulative incidence of local and systemic recurrence and mortality at 3 months, 1 and 2 years by surgical approach

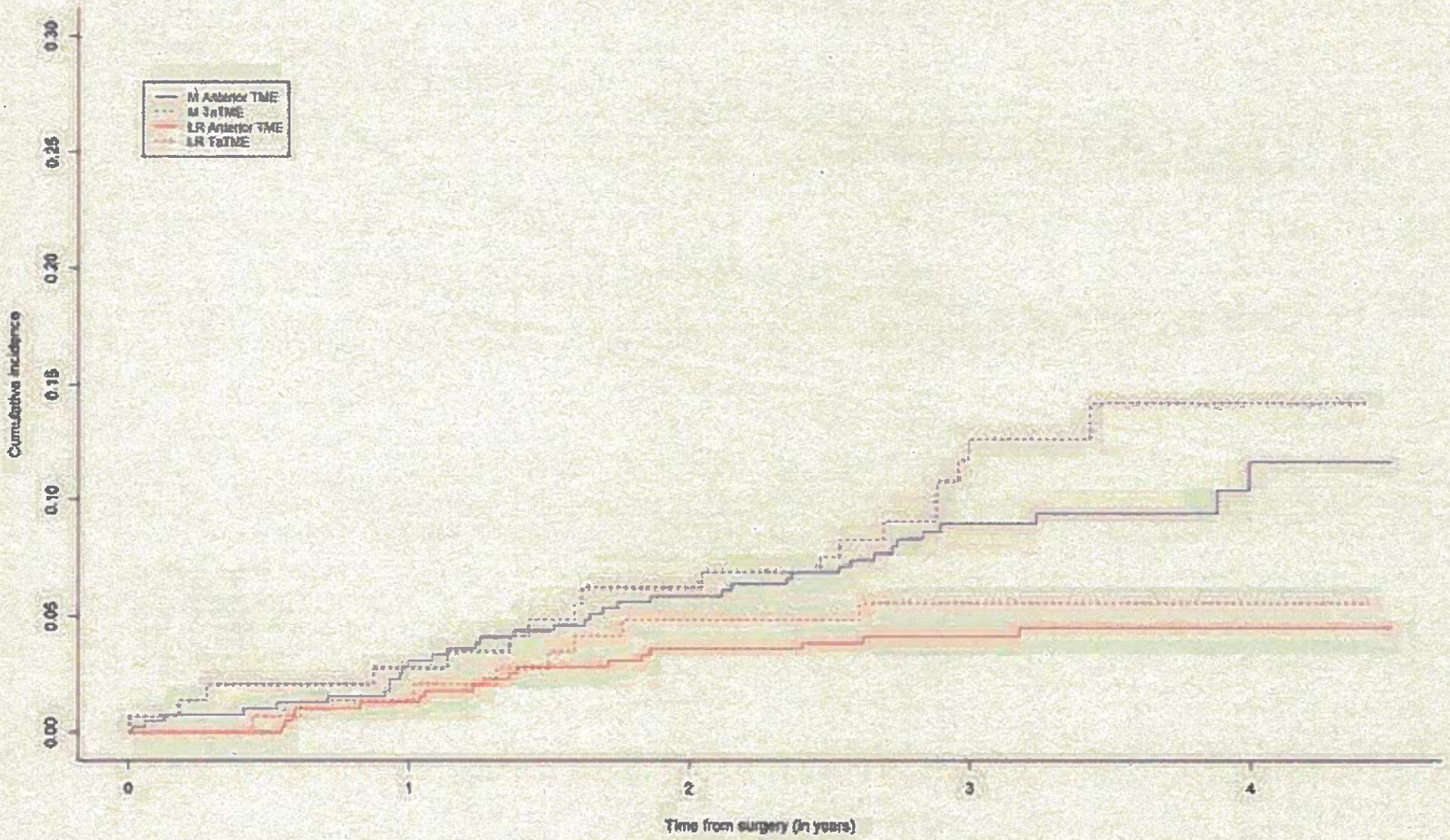
Time from surgery	Anterior TME			TaTME		
	LR	Systemic	Mortality	LR	Systemic	Mortality
3 months	0 [-]	1.28 [0.49; 2.81]	0.77 [0.21; 2.10]	0 [-]	1.38 [0.27; 4.49]	1.38 [0.27; 4.49]
1 year	1.28 [0.49; 2.81]	6.38 [4.24, 9.09]	2.3 [1.13; 4.16]	0.69 [0.06; 3.49]	11.03 [6.58; 16.77]	2.76 [0.91; 6.45]
2 years	3.57 [2.05; 5.76]	10.71 [7.90; 14.02]	3.57 [2.05; 5.76]	4.14 [1.70; 8.31]	15.86 [10.45; 22.29]	4.83 [2.13; 9.20]

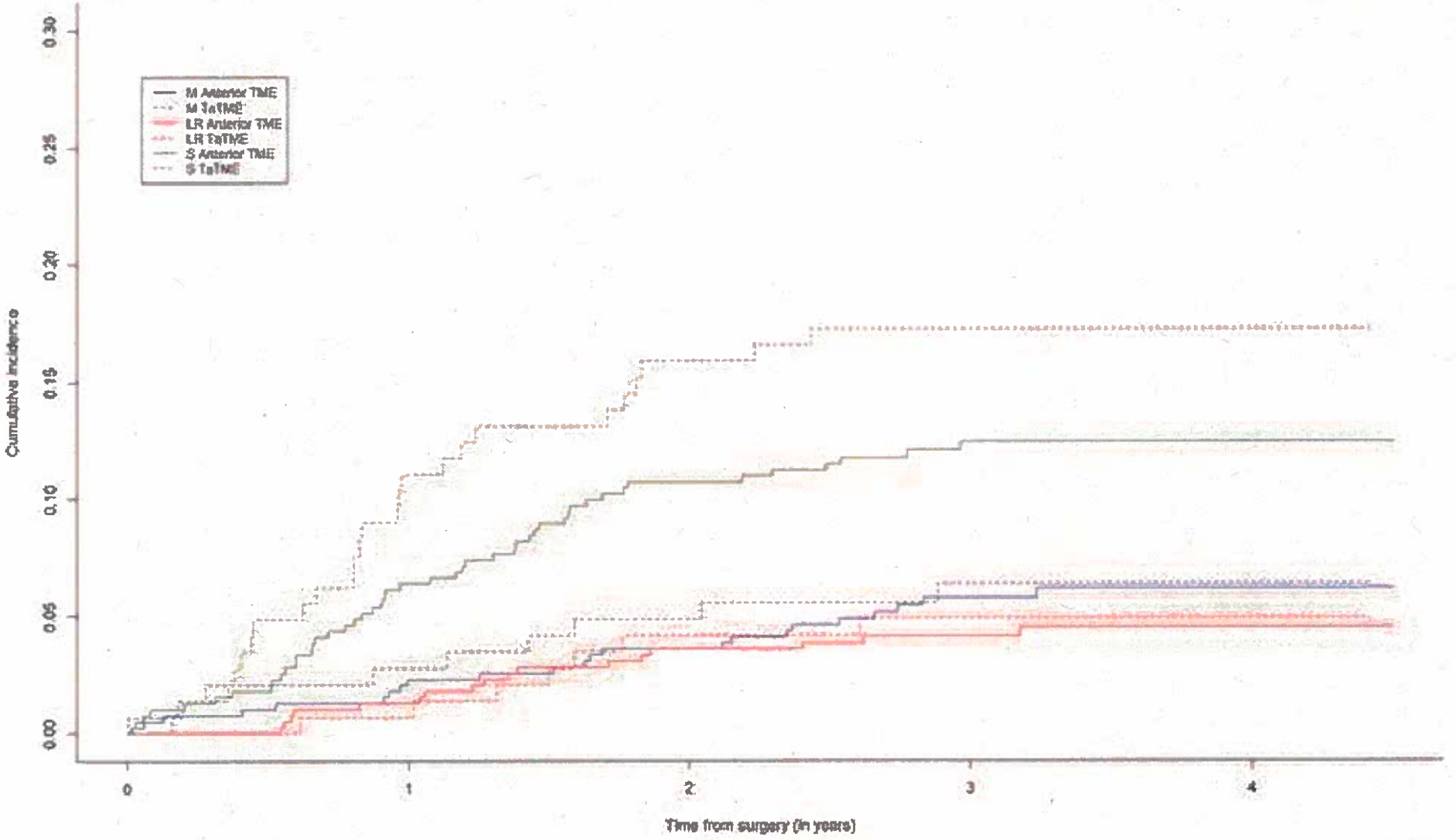
[95% Confidence Interval]

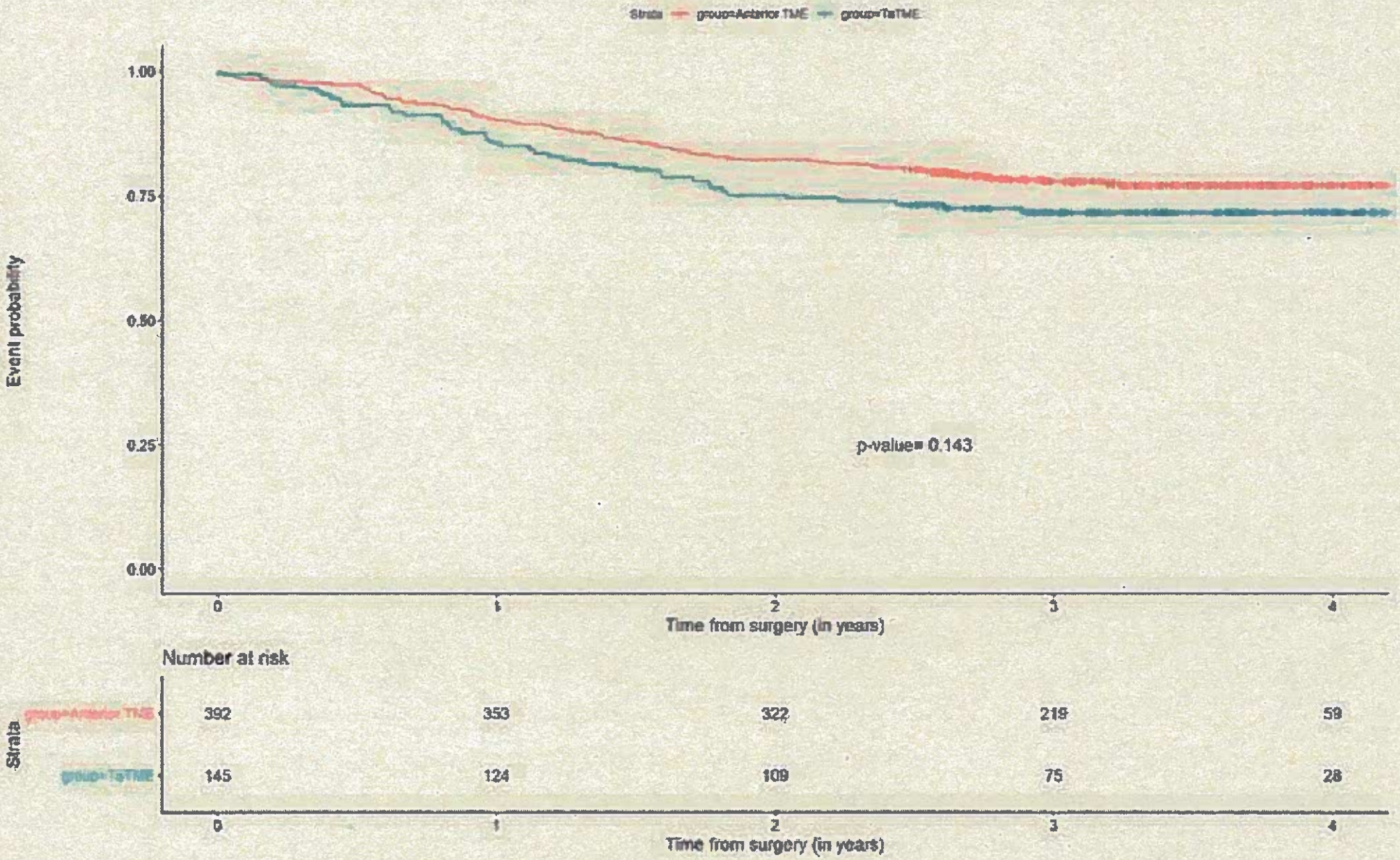
Figure 1. Flow chart showing selection of study participants

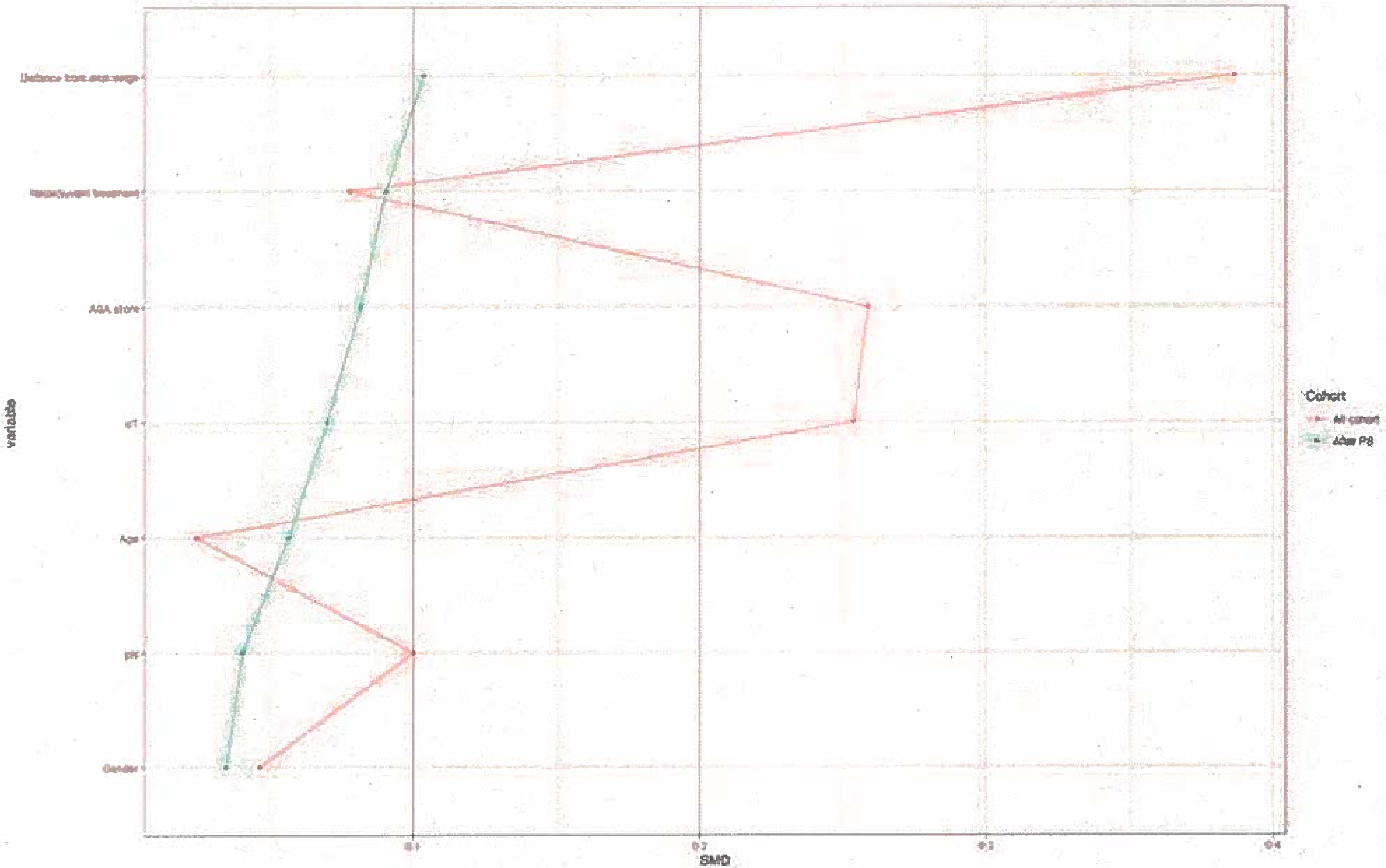


Catalonian Hospital Discharge Minimum Basic Data Set (HDMBD) 2. Transanal local excision 3. Transanal total mesorectal excision 4. Anterior total mesorectal excision 5. *See bar graph of contributing nters in supplementary materials*


M Anterior TME
M TaTME
LR Anterior TME
LR TaTME
Cumulative incidence
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0
1
2
3
4
Time from surgery (in years)


M Anterior TME
M TaTME
LR Anterior TME
LR TaTME
S Anterior TME
S TaTME
Cumulative incidence
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0
1
2
3
4
Time from surgery (in years)

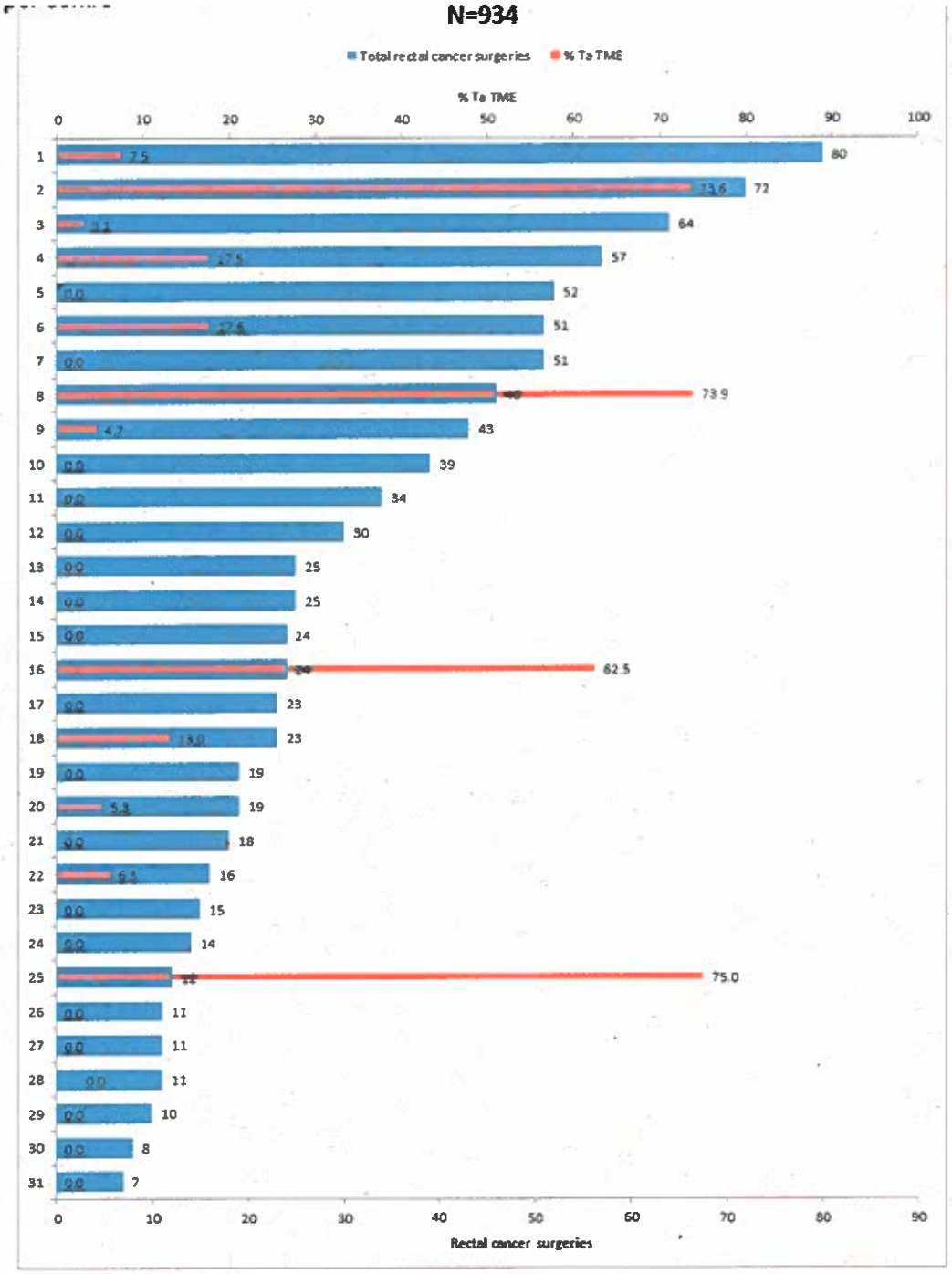

Strata
group=Anterior TME
group=TaTME
1.00
0.75
0.50
0.25
0.00
Event probability
p-value= 0.143
0
1
2
3
4
Time from surgery (in years)
Number at risk
Strata
group=Anterior TME
group=TaTME
392
353
322
219
59
145
124
109
75
28
0
1
2
3
4
Time from surgery (in years)



variable
ASA score
cT
Age
pN
Gender
0.1
0.2
0.3
0.4
SMD
Cohort
All cohort
After PS

Supplemental table. Location of local recurrences

Location	Anterior TME	Transanal TME
	N=17	N=8
Presacral	5 (29.4 %)	4 (50 %)
Anterior	2 (11.8 %)	2 (25 %)
Rectal stump	5 (29.4 %)	0
Anastomotic	1 (5.9 %)	0
Lateral	1 (5.9 %)	0
Not specified	3 (17.6 %)	1 (12.5 %)
Multiple sites	0	1 (12.5 %)


N=934
Total rectal cancer surgeries
% Ta TME
% Ta TME
0 10 20 30 40 50 60 70 80 90 100
1 7.5 80
2 73.6 72
3 3.1 64
4 17.5 57
5 0.0 52
6 27.5 51
7 0.0 51
8 73.9
9 4.7 43
10 0.0 39
11 0.0 34
12 0.0 30
13 0.0 25
14 0.0 25
15 0.0 24
16 62.5
17 0.0 23
18 13.0 23
19 0.0 19
20 5.3 19
21 0.0 18
22 6.3 16
23 0.0 15
24 0.0 14
25 75.0
26 0.0 11
27 0.0 11
28 0.0 11
29 0.0 10
30 0.0 8
31 0.0 7
0 10 20 30 40 50 60 70 80 90
Rectal cancer surgeries