



Oncological outcomes for transanal total mesorectal excision

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Abstract: Total mesorectal excision (TME) has become the gold standard technique for rectal cancer surgery with curative intent. Advantages in technology and surgical innovation lead to the introduction of minimally invasive techniques including laparoscopic, robotic and, more recently, transanal TME (TaTME). The concept of TaTME has been proposed to overcome the technical challenges encountered with the transabdominal approaches (open, laparoscopic, robotic) in the most difficult cases (obese, male patients with mid-low rectal cancer and a narrow, radiated pelvis and bulky mesorectum). Additionally, it has been recently claimed that TaTME offers at least 3 oncological advantages: (I) a longer distal resection margin (DRM), (II) a decreased rate of positive circumferential resection margin (CRM), (III) improved quality of TME. However, the oncological outcomes of TaTME compared to those of laparoscopic and robotic TMEs, remain controversial. Hence, a review of all the literature examining oncological outcomes after TaTME was performed. Two reviewers independently conducted a search of electronic databases (PubMed, MEDLINE, Cochrane Library). The last search was performed on August, 30th 2019. After the initial screen of 326 articles, 32 papers were selected for review, of these 19 were comparative studies and 1 a randomized controlled trial. TaTME resulted to provide oncologic outcomes at least comparable with the other minimally invasive approaches (laparoscopic, robotic) and seems to be associated with a lower rate of CRM involvement and TME incompleteness when compared to the laparoscopic, robotic, open approaches. Scarcity of data and short follow-up time made it impossible to draw conclusions on long-term oncologic outcomes. Hopefully, the COLOR III multicenter RCTs will shed a light on short- and long-term oncologic outcomes after TaTME.

Keywords: Transanal; total mesorectal excision (TME); laparoscopic; robotic; oncologic outcomes

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Introduction

Total mesorectal excision (TME) has become the gold standard technique for rectal cancer surgery with curative intent (1). Circumferential resection margin (CRM), distal resection margin (DRM) and quality of TME are the main histopathology metrics directly affecting local recurrence (LR) and cancer-specific survival rates (2).

Advantages in technology and surgical innovation lead to

the introduction of minimally invasive techniques including laparoscopic, robotic and, more recently, transanal TME (TaTME).

Obese, male patients with mid-low rectal cancers constitute a well-known challenge to low anterior resection with TME brought into even sharper relief when attempted laparoscopically. There are concerns that such patients with a narrow, radiated pelvis and bulky mesorectum may currently be undergoing sphincter-sparing resections

with an involved CRM, a poor quality TME, or even an unnecessary abdominoperineal resection (APR). The concept of TaTME has been proposed to overcome the technical challenges encountered with the transabdominal approaches (open, laparoscopic, robotic) in these more difficult cases.

Recent randomized controlled trials (3-6) and comparative studies (7-8) have reported similar short- and long-term oncological outcomes among open, laparoscopic and robotic approaches. It has been recently claimed that TaTME offers at least three oncological advantages: (I) a longer DRM thanks to the distal transection under direct visual control, (II) a decreased rate of positive CRM, (III) improved quality of TME. However, the oncological outcomes of TaTME compared to those of laparoscopic and robotic TMEs, remain controversial.

The aim of this review was to evaluate TaTME oncological outcomes.

Methods

A review of the literature was performed searching in PubMed, MEDLINE, and Cochrane Library until August 30th, 2019. Two reviewers (CF, AL) independently conducted a search on electronic databases (PubMed, MEDLINE, Cochrane Library) using the following search headings: (“laparoscopic TME” OR “lapTME”) AND (“TaTME”) OR (“robotic rectal surgery”); (“transanal TME”) OR (“taTME”) OR (“Transanal Total mesorectal Excision”); (“transanal” OR “transanal endoscopic microsurgery”) OR (“transanal minimally invasive surgery”) OR (“natural orifice transluminal endoscopic surgery”) OR (“NOTES”) AND (“Tatme oncological outcomes”).

The reference lists provided by the identified articles were additionally hand-searched to prevent article loss by search strategy. This method of cross-references was continued until no further relevant publications were identified. Inclusion criteria were prospective, retrospective, randomized, comparative studies about TaTME for rectal cancer. Exclusion criteria were: abstracts, letters, editorials, technical notes, expert opinions, reviews, meta-analysis, studies reporting benign pathologies, studies in which the outcomes and parameters of patients were not clearly reported, studies in which it was not possible to extract the appropriate data from the published results, overlap between authors and centers in the published literature, studies with inappropriate number of patients (<10); non-English language papers.

The literature search yielded 326 papers, after the filtering, 32 articles were selected. The process is listed in *Figure 1*.

Results

Among the 32 selected articles 13 were case series (9-21) and 19 comparative studies (22-40), of these one was a RCT (22). Year of publication ranged from 2014 (22-36) to 2019 (12,23,40). Mean distance of tumor from the anal verge was reported in 17 studies (10-12,17-20,22,26-28,34-38,40) and ranged from 2 (34) to 8 cm (36) for TaTME and from 1.5 (34) to 7 cm (26) in LapTME. *Table 1* gives a detailed overview of the selected studies.

Number of harvested nodes

Twenty-six out of 31 studies reported the mean number of harvested nodes which ranged from 10.7 (28) to 26.45 (26) in TaTME; from 11 (28) to 26.69 (26) in laparoscopic TME (LapTME) and from 13 (17) to 16.8 (18) in robotic TME (RobTME). The mean number of harvested nodes after open TME (OpTME) was reported in 1 study and was 23.5±8.2 (7).

One (31) of the 16 comparative studies (22,24-34,36, 38-40) reported statistically significant difference in number of harvested nodes between Ta- and OpTME but no difference was reported when Ta- and LapTME were compared. *Table 2* shows the results in details.

DRM

Twenty-five (9-15,17-20,22,24-28,31-34,36,38-40) out of 31 studies reported the DRM which ranged from 1 cm (3,10,14,29) to 2.8 cm (24) in TaTME. The mean length of DRM after LapTME was available in 10 (22,24,25,31,33-36, 38-40) studies and ranged from 1 cm (10) to 2.5 cm (36). The mean length of DRM after RobTME was reported in 4 (26-28,32) articles and ranged from 1.5 cm (27) to 3.1 cm (32). DRM after OpTME was reported in 2 studies (31,40) and was 1.6 and 3.47 cm (31,40).

Five (6,25,27,31,32) out 18 (24,31-33,39) comparative studies reported statistically significant difference in mean length of DRM. Three studies reported significantly longer mean DRM after TaTME *vs.* Lap TME (6,25,27). One study (32) reported longer DRM after Rob TME *vs.* TaTME. Perdawood *et al.* (31) reported longer DRM when TaTME or LapTME where compared to OpTME, but no

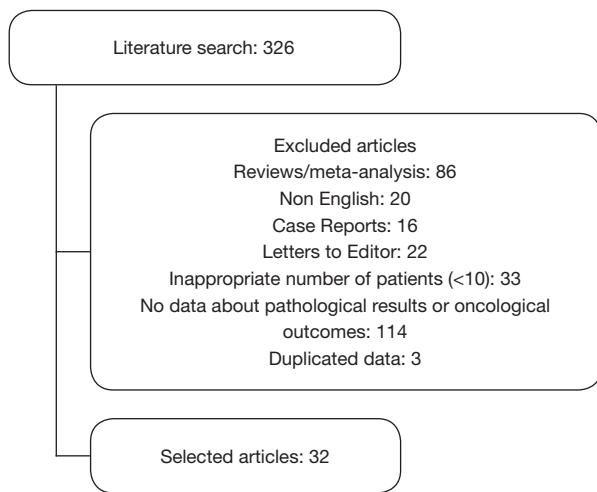


Figure 1 Flow diagram of literature search.

difference was reported between TaTME and LapTME. Six comparative studies (22,25,27,30,31,34) reported the DRM involvement rate which ranged from 0% to 8% in the TaTME and LapTME cases, DRM was involved in 0.3% of RobTME in the only study reporting this data (27). No statistically significant difference was reported among studies in DRM involvement rates. *Table 2* shows the results in details.

CRM

CRM involvement after TaTME surgery were reported in 27 studies (*Table 2*). And ranged from 0% (15,24,26,33,38,40) to 12% (30) after TaTME, from 0% (24,33,35) to 13% (31) in 7 studies (22-25,29-31)

Table 1 Studies overview

Reference	Year	Country	Study design	TaTME (n)	Lap TME (n)	RobTME (n)	OpTME (n)	Mean distance from anal verge (cm)
Abdelkader <i>et al.</i> (9)	2018	Egypt	Case series	25				
Buchs <i>et al.</i> (10)	2016	United Kingdom	Case series	40				3 (0–10)
Burke <i>et al.</i> (11)	2016	United States	Case series	50				4.4 (3.0–5.5)
De Rosa <i>et al.</i> (12)	2019	Italy	Case series	12				6.25 (3.5–10)
de Lacy <i>et al.</i> (13)	2018	Spain	Case series	186				
Hüscher <i>et al.</i> (14)	2016	Italy	Cases series	102				
Kang <i>et al.</i> (15)	2015	China	Cases series	20				
Lacy <i>et al.</i> (16)	2015	Spain	Cases series	140				
Muratore <i>et al.</i> (17)	2015	Italy	Cases series	26				4.4 (3–6)
Park <i>et al.</i> (18)	2018	Korea	Cases series	49				6.3±2.2
Penna <i>et al.</i> (19)	2017	United Kingdom	Cases series	720				3.0 (0–11)
Rottoli <i>et al.</i> (20)	2015	United Kingdom	Cases series	11				5 (2–7)
Veltcamp <i>et al.</i> (21)	2016	Netherlands	Cases series	80				
Denost <i>et al.</i> (22)	2014	France	Comparative RCT	50				4 (2–6)
					50			4 (2–6)
Detering <i>et al.</i> (23)	2019	Netherlands	Comparative	396	396			
Fernández-Hevia <i>et al.</i> (24)	2015	Spain	Comparative	37	37			
Kanso <i>et al.</i> (25)	2015	France	Comparative	51	34			
Law <i>et al.</i> (26)	2018	Hong Kong	Comparative	40				5 (2–10)
						40		7 (2–15)

Table 1 (continued)

Table 1 (continued)

Reference	Year	Country	Study design	TaTME (n)	Lap TME (n)	RobTME (n)	OpTME (n)	Mean distance from anal verge (cm)
Lee L <i>et al.</i> (27)	2018	Multicenter	Comparative	226		370		5.6 (2.5)
Lee KY <i>et al.</i> (28)	2018	Korea	Comparative	26				6.1±1.63
						36		5.2±1.99
Lelong <i>et al.</i> (29)	2016	France	Comparative	34	38			
Mege <i>et al.</i> (30)	2018	United States	Comparative	23	34			
Perdawood <i>et al.</i> (31)	2018	Denmark	Comparative	100	100		100	
Perez <i>et al.</i> (32)	2017	Germany	Comparative	55	60			
Persiani <i>et al.</i> (33)	2018	Italy	Comparative	48	57			
Roodbeen <i>et al.</i> (34)	2018	Multicenter	Comparative	41				2.0 (0.0–4.0)
					41			1.5 (0.0–3.0)
Rubinkiewicz <i>et al.</i> (35)	2018	Poland	Comparative	35				2.9±1.17
					35			3.19±1.47
Velthuis <i>et al.</i> (36)	2014	Netherlands	Comparative	25				8
					25			6
Caycedo-Marulanda <i>et al.</i> (37)	2018	Canada	Comparative	43				6.80±2.09
Chang <i>et al.</i> (38)	2018	Taiwan	Comparative	23				4.3±1.4
					23			5.9±1.1
Chen CC <i>et al.</i> (39)	2016	Taiwan	Comparative	50	100			
Chen YT <i>et al.</i> (40)	2019	Taiwan	Comparative	39				4.3±1.4
					64			5.8±1.2
							23	5.6±1.3

TME, total mesorectal excision; TaTME, transanal TME; LapTME, laparoscopic TME. RobTME, robotic TME; OpTME, open TME.

reporting LapTME, from 5% (26) to 8.3% (28) in 3 studies reporting RobTME (26-28) and was 10% (31) and 13% (40) in 2 studies reporting OpTME (31,40). Three studies reported significantly lower CRM involvement rates in TaTME *vs.* LapTME (22,38,40) or OpTME (40). Among these 3 studies (22,38,40), one was a RCT (22) comparing the transanal and laparoscopic approach. The cut-off to define a positive CRM was 1 mm in 25 studies (9-11,13,15,16,18,19,22-31,33-35,37-40) and 2 mm in 2 studies (21,36). Eighteen studies (10-17, 19,20,22,24,25,31,32,34,36,39) reported the CRM width in mm, of these 8 were comparative (22,24,25,31,32,34,36,39). CRM width ranged from 5 mm (20) to 37.1 mm (14) in TaTME, from 5 (22,34) to 12 mm (24,36) in LapTME. One

study reported the width of CRM in the OpTME (31) and another in the RobTME (32). This last study (32) reported a statistically significant wider CRM in the RobTME *vs.* the TaTME group. *Table 2* shows the results in details.

Quality of TME

Quality of TME according to Quirke (41) was evaluated in 23 studies (9,11-18,21,22,24,27-37) [12 comparative (22,24,27-36)]. Complete quality of specimen ranged from 53% (30) to 100% (12) after TaTME, from 52.6% (29) to 92% (24) in the 9 studies evaluating LapTME (22,24,29-31, 33-37), from 88% (32) to 100% (28) in the 3 studies reporting RobTME (27,28,32) and was 68% in one study

Table 2 Oncological outcomes

Reference	Pts	Surgical technique	Harvested nodes	Distal margin distance (cm)	CRM + (%)	CRM (mm)	Complete TME	Nearly complete TME	Incomplete TME
Abdelkader <i>et al.</i> (9)	25	TaTME		1.9±1.1	2 (8)		22 (88)	2 (8)	1 (4)
Buchs <i>et al.</i> (10)	40	TaTME	20±9.7	2.69±2.22	2 (5)	10.8±9.5			
Burke <i>et al.</i> (11)	50	TaTME	18.0 (12.0–23.8)	1.0 (0.5–1.7)	2 (4)	7.0 (2.5–15.0)	36 (72)	13 (26)	1 (2)
De Rosa <i>et al.</i> (12)	12	TaTME	13.6±6.6	2.08±1.42		16.1±7.6	12 (100)	0	0
de Lacy <i>et al.</i> (13)	186	TaTME	14.0	2.1	7 (10.1)	15.4	178 (95.7)	3 (1.6)	2 (1.1)
Hüscher <i>et al.</i> (14)	102	TaTME	20±11.7	3.71±2.85		37.1±28.5	99 (97.1)	3 (2.9)	
Kang <i>et al.</i> (15)	20	TaTME		1.0 (0.5–2.5)	0 (0)	12 (3–19)	18 (90)	2 (10 %)	0
Lacy <i>et al.</i> (16)	140	TaTME	14.7±6.8		9 (6.4)	22±4	136 (97.1)	3	1
Muratore <i>et al.</i> (17)	26	TaTME		1.9		11.1	23 (88.4)		
Park <i>et al.</i> (18)	49	TaTME	19 (8–42)	2.4±0.19	4 (8.2)		35 (71.4)	12 (24.5)	2 (4.1)
Penna <i>et al.</i> (19)	720	TaTME	16.5±9.2	1.9±1.43	14 (2.4)	9.19±8.6			
Rottoli <i>et al.</i> (20)	11	TaTME	21.7 (11–50)	1 (0.5–2.0)		5 (1–20)			0
Veltcamp <i>et al.</i> (21)	80	TaTME	14 (6–30)	Positive DRM: 0%	2 (2.5) ^c		71 (88)	7 (9)	2 (3)
Denost <i>et al.</i> (22)	50	TaTME	17 (2–30)	1 (0–3) ^s	2 (4)	7 (0–20)	35 (70)	9 (18)	6 (12)
	50	LapTME	17 (9–40)	1 (0.1–3) ^s	9 (18)	5 (0–20)	31 (62)	13 (26)	6 (12)
Detering <i>et al.</i> (23)	396	TaTME			17 (4.3)				
	396	LapTME			16 (4.0)				
Fernández-Hevia <i>et al.</i> (24)	37	TaTME	14.3±6	2.8±1.8	0	11±0.6	35 (95)	2 (5)	0
	37	LaTME	14.7±6	1.7±1.3	0	12±0.9	34 (92)	2 (5)	1 (3)
Kanso <i>et al.</i> (25)	51	TaTME	15±8	1.2±0.9 [^]	5 (10)	7±6			
	34	LapTME	13±7	1.8±1.5 [^]	3 (9)	7±6			
Law <i>et al.</i> (26)	40	TaTME	13	2 (0.5–5)	0 (0)				
	40	RobTME	13	2 (0.5–6)	2 (5)				
Lee L <i>et al.</i> (27)	226	TaTME	16.1	1.69 ^l	12 (6.3)		209 (92.5)	15 (6.6)	2 (0.9)
	370	RobTME	16.8	1.51 ^l	21 (6.2)		356 (95.4)	14 (3.8)	3 (0.8)
Lee KY <i>et al.</i> (28)	21	TaTME	10.7±6.28	2.2±1.28	1 (4.8)		19 (90.5)	2 (94.5)	0
	24	RobTME	13.6±6.29	1.9±1.06	2 (8.3)		24 (100)	0	0
Lelong <i>et al.</i> (29)	34	TaTME	14 (6–34)		2 (5.8)		19 (55.8)	15	0
	38	LapTME	12 (4–25)		4 (10.5)		20 (52.6)	16	2
Mege <i>et al.</i> (30)	34	TaTME	14±10	Positive DRM TaTME 1 (3%) vs. LapTME 1 (3%) P=1	4 (12)		18 (53)	9 (27)	7 (21)
	34	LapTME	14±8		2 (6)		27 (79)	3 (9)	4 (12)

Table 2 (continued)

Table 2 (continued)

Reference	Pts	Surgical technique	Harvested nodes	Distal margin distance (cm)	CRM + (%)	CRM (mm)	Complete TME	Nearly complete TME	Incomplete TME
Perdawood <i>et al.</i> (31)	100	TaTME	22.32±8.70 [#]	2.22±1.27 [”]	7 (7)	8.99±7.21	58 (58) [§]	28 (28) [§]	14 (14) [§]
	100	LapTME	21.75±10.98 [#]	2.40±1.51 [”]	13 (13)	9.44±7.86	68 (68) [§]	12 (12) [§]	20 (20) [§]
	100	OpTME	17.92±9.29 [#]	3.47±2.35 [”]	10 (10)	9.57±7.49	68 (68) [§]	15 (15) [§]	17 (17) [§]
Perez <i>et al.</i> (32)	55	TaTME	15 (8–55)	1.9 (0.8–3)		12 (5–20)	50 (91)	5 (9)	0
	60	RobTME	15 (7–30)	3.1 (1.9–4.5)		19 (12–49)	53 (88)	7 (12)	0
Persiani <i>et al.</i> (33)	48	TaTME	12 (3–26)	2.5 (0.5–6)	0		40 (87)	4 (8.7)	2 (4.3)
	57	LapTME	11 (3–26)	1.5 (0.5–4)	0		39 (84.8)	5 (10.9)	2 (4.3)
Roodbeen <i>et al.</i> (34) ^ε	41	TaTME	18 (13–26)	2 (1–4)	3 (7)	10 (4.2–12)	38 (92.7)		
	41	LapTME	14 (11–24)	2 (0.98–4.13)	2 (4.8)	5 (3–10)	21 (84.0)		
Rubinkiewicz <i>et al.</i> (35)	35	TaTME		Positive DRM 0 TaTME vs. 1 (2.8%) LapTME	1 (2.8)		31 (89)	4 (11)	0 (0)
	35	LapTME			0		29 (83)	6 (17)	0 (0)
Velthuis <i>et al.</i> (36)	25	TaTME	14 (7–24)	2.3 (0.5–8)	1 (4) ^ε	13 (1.5–3)	24 (96)	1 (4%)	0
	25	LapTME	13 (1–36)	2.5 (0–5.5)	2 (8) ^ε	12 (0–2.5)	18 (72)	2 (8%)	5 (20)
Caycedo-Marulanda <i>et al.</i> (37)	43	TaTME	24.81±9.90		1 (2.33)		36 (83.72)	7 (16.28)	0
Chang <i>et al.</i> (38)	23	TaTME	22.8±10.8	1.35±1.05	0 (0)				
	23	LapTME	19.5±8.6	1.55±1.05	4 (7)				
Chen CC <i>et al.</i> (39)	50	TaTME	16.7±7.8	2.4±1.2	2 (4)	11.8±7.5			
	100	LapTME	17.4±8.9	1.5±0.9	10 (10)	11.1±7.7			
Chen YT <i>et al.</i> (40)	39	TaTME	20.8±9.0	1.6±1.4	0*				
	64	LapTME	18.8±8.1	1.9±1.3	5 (7.8)*				
	23	OpenTME	23.5±8.2	1.6±0.9	3 (13)*				

*, TaTME vs. LapTME P=0.08; TaTME vs. OpTME P<0.01; Lap TME vs. OpTME P=0.2; [§], positive DRM TaTME 1 (2%) vs. LapTME 4 (8%) P=0.362; [^], positive DRM TaTME 4 (8%) vs. LapTME 0 P=0.25; [†], positive DRM TaTME 4 (1.8%) vs. RobTME 1 (0.3%) P=0.051; [#], TaTME vs. LapTME P=0.889; TaTME vs. OpTME P=0.003; LapTME vs. OpTME P=0.018; [“], TaTME vs. LapTME P=0.995; TaTME vs. OpTME P<0.065; LapTME vs. OpTME P=0.052; positive DRM TaTME 0, LapTME 1, OpTME 1 P=0.604; [§], TaTME vs. LapTME P=0.016; TaTME vs. OpTME P=0.082; LapTME vs. OpTME P=0.750; ^ε, positive DRM TaTME 0 vs. Lap TME 3 (7%) P=0.241; ^ε, positive CRM <2 mm. TME, total mesorectal excision; TaTME, transanal TME; LapTME, laparoscopic TME. RobTME, robotic TME; OpTME, open TME.

reporting OpTME (31). Incomplete quality of TME ranged from 0% (12,15,20,24,28,29,32,35–37) to 21% (30) in TaTME, from 0% (28,35) to 20% (31,36) in LapTME and was 0% in the 2 studies reporting RobTME (28,32) and 17% in one study reporting OpTME (31). Two (31,36) out of the 12 comparative (22,24,27–36) studies reported a statistically significant higher rate of complete TME with TaTME vs. LapTME. Table 2 shows the results in details.

Long-term survival

Eight studies (9,10,11,16,21,25,27,40) reported long term follow-up data, of these 3 were comparative (25,27,40). Follow-up time was reported in median (15.1–39 months) (11,25,27) or mean (15–28.6 months) (9,10,16). LR, DFS and OS rates after TaTME ranged from 0% (40) to 4.8% (27), from 63% (25) to 90.8% (16) and from 92.5% (10) to

Table 3 Long-term oncologic outcomes

Reference	Patients	Surg technique	Follow-up (months)	Local recurrence (%)	DFS	OS
Abdelkader <i>et al.</i> (9)	25	TaTME	28.6±5.9 (7–36) mean	1 (4)	22 (88)	
Buchs <i>et al.</i> (10)	40	TaTME	6.5 mean		34 (85)	37 (92.5)
Burke <i>et al.</i> (11)	50	TaTME	15.1 (7–23.7) Median	2 (4)	41 (82) ^ε	
Lacy <i>et al.</i> (16)	140	TaTME	15±9.1 mean	1 (0.8)	119 (90.8)	136 (97.1)
Veltcamp <i>et al.</i> (21)	80	TaTME	30	2 (2.5)		
Kanso <i>et al.</i> (25)	51	TaTME	39 (0–85)		32 (63)	51 (100)
	34	LapTME	Median		21 (62)	32 (93)
Lee <i>et al.</i> (27)	21	TaTME	20.1	1 (4.8)		
	24	RobTME	22 median	0 (0)		
Chen YT <i>et al.</i> (40)	39	TaTME	24	0 (0)	2 (90)*	2 (97)
	64	LapTME		3 (4.7)	2 (91)*	2 (89)
	23	OpenTME		2 (8.7)	2 (65)*	2 (89)

*, TaTME vs. LapTME P=0.7; TaTME vs. Op TME P=0.01; LapTME vs. OpTME P=0.01; ^ε, 2 patients already metastatic at diagnosis. TME, total mesorectal excision; TaTME, transanal TME; LapTME, laparoscopic TME.

100% (25) respectively. Chen *et al.* (40) reported a statistically higher DFS when TaTME and LapTME were compared to OpTME (P=0.01), no difference in DFS was reported when taTME was compared to LapTME (P=0.7). *Table 3* shows the results in details.

Discussion

The gold standard treatment for mid-low rectal cancers is TME, which has been elucidated to optimize locoregional clearance (1) and to decrease LR rates (42).

Laparoscopic and robotic TME represent a leap forward in the treatment of rectal neoplasms, providing improved short-term and analogous long-term outcomes (3-8,43). However, performing an anterior rectal resection with a good quality TME is technically challenging, particularly with the laparoscopic approach, due to the tapering of the distal mesorectum and inadequate identification of the neurovascular bundle, and mainly because of the limited operative field leading to a difficult view and difficult placement of endoscopic staplers and mobilization in the deep pelvis. Aforementioned factors in combination with suboptimal anastomotic techniques evoke insufficiency of DRM, incompleteness of mesorectum and CRM involvement, with consequent LR. Previous RCTs (3,44)

found a high involvement of CRM rate (7–12.1%) in laparoscopic TME. The ROLARR trial (8) found no statistically significant oncological or clinical advantage of RobTME over LapTME with positive CRM rates of 5.1% and 6.3% respectively. The “bottom-up” approach of TaTME was pioneered to minimize the limits of the “up-to-down” approaches. In fact, TaTME helps to clearly expose the anatomical plane and accurately determine the resection margin in a narrow pelvis, as well as a more direct approach to the most problematic aspects of the distal rectal dissection, thus in turn producing better perioperative results, enhanced oncological quality as well as superior nerve-sparing (45,46).

This review was focused on the quality of TME, DRM and CRM as they are the measures of the TME quality and are deemed as major predictive factors for rectal resections affecting LR and survival (1,41,47). TaTME resulted to provide good oncologic outcomes and seems to be associated with a lower rate of CRM involvement and TME incompleteness when compared to the abdominal approaches (laparoscopic, robotic, open). These results were also reported by two recent meta-analysis comparing one Ta- and LapTME (48) and the other Ta-, Rob- and OpTME (49). Ma *et al.* (50) in their systematic review and meta-analysis reported longer CRM, less positive CRM

rates and a higher rate of complete specimens when TaTME was compared with LapTME. Another meta-analysis analysing Ta- and RobTME (51) reported lower pooled CRM involvement rates for TaTME, although this result was not statistically nor clinically significant. Accordingly, the only RCT (22) comparing Ta- and LapTME reported a significantly lower CRM involvement rate with the bottom-up approach.

It is undeniable that the core value of TaTME lies in achieving an adequate DRM as the rectal transection is under direct visual control. Nonetheless, there was no significant difference among studies in terms of DRM as reported also by a recent meta-analysis (51). Surprisingly, one study (32) reported significantly lower DRM and CRM in the TaTME group when compared to the robotic approach although there were no differences among the two groups in tumor size and site, neoadjuvant therapy or Quirke's mesorectal grading. However, a possible institutional bias with different pathological assessment of the specimens may have affected the results. For this reason, result pertaining DRM should be interpreted cautiously as it is important to point out the heterogeneity of the published studies in terms of tumor size and tumor stage and mainly of tumor location (48,50,51).

A study by Perdawood *et al.* (52) aiming to compare 29 TaTME to 29 LapTME cases with defects in the retrieved specimen reported a significantly longer DRM in the TaTME group (33.45+14.5 *vs.* 25.41+11.16; P=0.048). Interestingly, the ratio of defects below the peritoneal reflection was significantly lower in the TaTME group suggesting that TaTME has the potential to improve rectal cancer surgery through improvement of dissection in the lower rectum.

It is important to note that most of the reported studies included the surgeon's learning curve and despite this, results were very promising.

Most studies have reported only short-term outcomes, which reflects the novelty of TaTME. Whether this new approach has similar oncological outcomes in terms of LR, DFS and cancer specific survival will require further studies in prospective trials that compare TaTME with laparoscopic or robotic TME over substantial follow-up period.

As TaTME is adopted increasingly by surgeons, patients' selection criteria will be crucial to continue to animate the debate. Hopefully, the TaTME international registry as well as COLOR III RCT (53) with its strict selection criteria will give definitive answers on short- and long-term oncologic outcomes after TaTME (*vs.* lapTME).

Conclusions

TaTME is an oncologically safe and effective technique, resulting in at least comparable oncologic outcomes when compared to the abdominal approaches. Standardization of surgical technique, implementation in daily practice as well as strict selection criteria are required to further clarify the role of TaTME in the treatment of rectal cancer. Hopefully, the COLOR III multicenter RCTs will shed a light on short- and long-term oncologic outcomes after TaTME.

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