Transanal total mesorectal excision in rectal cancer: why, how and when

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Practice points

- Up-to-down total mesorectal excision (TME) is the gold-standard approach to rectal cancer.
- Up-to-down TME is technically demanding in patients with narrow pelvis or low rectal cancer.
- Down-to-up TME or transanal TME (taTME) seems to increase the oncological safety in patients with mid-low rectal cancer.
- taTME seems to improve the quality of the mesorectal excision.
- taTME seems to decrease the rate of positive radial resection margins in patients with low rectal cancer.
- Patients with narrow pelvis or low rectal cancer may benefit more from the down-to-up approach.
- Studies with longer follow-up and larger cohort of patients are needed to draw more conclusive results about taTME approach.

Down-to-up total mesorectal excision (TME) or transanal TME (taTME) has gained worldwide popularity. taTME is one of the most promising innovations of the last years in the field of gastrointestinal surgery. Due to the better view of the dissection planes even in difficult patients (i.e., narrow pelvis or low rectal cancer), taTME seems to achieve both better TME quality reducing the rate of incomplete TME and lower rates of positive circumferential resection margins. taTME has overall morbidity and anastomotic leak rates comparable with the up-to-down TME. Mid-term results of taTME seems to be comparable with those of the up-to-down approach but definitive conclusions cannot be drawn since the short follow-up and small cohort of patients of the present studies.

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Up-to-down total mesorectal excision (TME) is the gold-standard approach to mid-low rectal cancers with 65% rates of 5 years survival and 6–10% rates of local recurrence [1]. Laparoscopic up-to-down TME is safe with short- and long-term results comparable with the open approach [2–4]. However, up-to-down TME for mid-low rectal cancers is technically and oncologically demanding, mainly in obese and male patients with a narrow pelvis; obtaining adequate resection margins as well as good quality TME specimens in this subset of patients is challenging [5,6]. Moreover, two European studies have recently highlighted the difficulty in performing laparoscopic up-to-down TME, analyzing almost 2000 patients operated on for rectal cancer in a short-time period: less than 15% out of almost 2000 patients with rectal cancer had a laparoscopic TME [7,8].
In 1995, Bannon et al. reported on their preliminary experience of ‘open’ down-to-up TME in 65 patients with low rectal cancer [9]. More recent papers have suggested that ‘open’ down-to-up TME reduces the risk of positive resection margins, either distal or radial, and increases the number of sphincter-saving procedures in low rectal cancer patients [10,11]. In 2010, the first case of laparoscopic down-to-up TME or transanal TME (taTME) was reported [12]. Since this report, laparoscopic down-to-up TME has gained popularity all over the world. Besides the lower rates of positive resection margins, the perceived benefits of the laparoscopic taTME seem to include ease of procedure and better TME quality due to better view of the dissection planes [13–15].

### Why switching from up-to-down TME to down-to-up TME?

#### TME quality

Down-to-up TME, either open or laparoscopic, is technically demanding, especially when performed in patients with a narrow pelvis (usually male), in obese patients or in patients with a low rectal cancer [5,6,8]. In this subset of patients, obtaining an adequate view of the dissection plane may be extremely difficult, jeopardizing the integrity of the mesorectal fascia. It is well known that non-complete TME excision is correlated with higher recurrence rates [16]. The first advantage of the down-to-up TME is a better view of the dissection planes and, as a consequence, a better quality of mesorectal excision (Table 1). In the series approaching the rectum from up-to-down, the rate of incomplete TME ranges from the 3% rate of the COLOR II study, with only 17% of the patients having a cancer located in the low rectum, to the 9.5% rate of the study from Marinello et al., reporting a 42% rate of patients with low rectal cancer [2,13,17]. When the down-to-up approach is used, despite higher numbers of low rectal cancer patients, the rate of incomplete TME decreases to 3% or less [13,15].

#### Resection margins

Both open and laparoscopic up-to-down TME are technically demanding when the cancer is located in the lower rectum. The technical difficulty is due to the anatomy of the anorectal canal and of the pelvic floor which have been described as a ‘tunnel in a funnel’. Thereafter, obtaining adequate resection margins, in particular radial resection margins, may be tricky especially in male patients with a deep narrow angulated pelvis. In a recent prospective study from a single Sweden center, the distance from the anal verge was significantly lower in the patients with positive circumferential resection margins (CRM ≤1 mm) than in those with negative CRM: 4.3 versus 8 cm, respectively (p = 0.001) [19]. In effect, three recent series have reported rate of positive circumferential resection margin in up to 15% of the patients with low rectal cancer approached transabdominally (up-to-down TME) (Table 2) [3,11,20]. Using the transanal approach, the dissection of the distal part of the rectum seems to be more favorable from an oncological point of view, since the better view and the possibility of carrying the dissection posteriorly to the levator ani fascia.

In a French study, 100 patients with low rectal cancer suitable for a low anterior resection were randomized between ‘open’ down-to-up TME and up-to-down TME [11]; the rate of positive circumferential resection margins was significantly lower in the down-to-up group: 4 versus 8% (p = 0.025). Similar low rates of positive circumferential resection margins have been reported by Mark et al. (‘open’ down-to-up TME in 106 patients) and by Tuech et al. (laparoscopic up-to-down TME in 56 patients) [10]. In our series of 43 patients with low rectal cancer who underwent laparoscopic down-to-up TME, the rate of positive circumferential resection margin was 2.4%. Recently, Kaneko et al. have reported on 85 patients with low rectal cancer who underwent low anterior resection with intersphincteric resection (down-to-up approach in 51 patients): no differences in terms of positive distal and circumferential resection margins were found according to the type of approach [20]. However, in both groups a transanal dissection was conducted; the only differences were the timing (as first step in the down-to-up approach) and the upward extension (up to 6 cm in the down-to-up approach, only intersphincteric dissection in the up-to-down approach).

Regarding the rate of positive distal resection margins, the type of approach (down-to-up versus up-to-down TME) does not seem to make any difference when dealing with cancers located in the lower rectum (Table 2). However, when dealing with cancers located in the mid rectum, Fernandez-Hevia et al. reported significantly longer distal resection margins in the taTME group compared with the conventional laparoscopic up-to-down group: 3.2 versus
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PERSPECTIVE

One possible explanation is that during the down-to-up approach for mid-rectal cancer, after inserting the single-port device into the anus, the lower edge of the cancer is clearly seen and the point where to do the purse-string suture of the rectal lumen and the transection of the rectal wall are done distally to the lower edge of the cancer and under direct vision. On the contrary, during the conventional up-to-down approach, the clear identification of the distal cancer margin is often inaccurate. Moreover, even if the location of the cancer can be identified either by inspection or by intraoperative endoscopy, positioning the stapler well below the lower edge of the tumor is difficult, especially in male patients with a narrow pelvis.

When transanal TME

• Short-/mid-term results & indications

As shown in Table 3, the down-to-up approach in mid-low rectal cancer has morbidity rates comparable with the up-to-down approach. The only randomized study comparing these two approaches has reported similar rates of postoperative complications: 44% in the up-to-down group versus 32% in taTME group (p = 0.2) [11]. When analyzing the rate of anastomotic leak, the down-to-up approach did not seem to increase the risk of leakage compared with the gold-standard transabdominal approach.

Most of the studies do not report major intraoperative complications during the transanal time of the procedure [13,15,20]. However, Rouane has recently reported two cases of urethral injury which occurred at the beginning of their experience: the first patient had a bulky rectal cancer and the second one a prostatic cancer, hindering the anterior plane of dissection. In our experience, the only intraoperative complication was bladder perforation in a patient previously undergone radical prostatectomy; the injury was repaired transanally and the postoperative stay was regular [28].

Most of the papers reporting on the oncological long-term results of the taTME approach have obviously shorter follow-up and smaller cohort of patients when compared with the papers analyzing the up-to-down approach. This bias hinders partially the results (Table 3). However, with median follow-up reported ranging from 15 to 39 months, the overall survival and local recurrence rates seem to compare favorably with those reported by the up-to-down approach studies.

There are lack of data about functional outcome after taTME. However, there are papers reporting the functional results after transanal endoscopic microsurgery: despite the use of a 4 cm in size metallic tube and operating times up to 150 min, no long-term effects on anorectal function or quality of life have been reported [29,30]. A recent paper has analyzed the functional results of transanal minimally invasive surgery for rectal polyps [31]. The Fecal Incontinence Severity Index questionnaire was completed at 3, 6, 9 and 12 months after transanal minimally invasive surgery: functional results were comparable with the transanal endoscopic microsurgery procedure.

Based on the available data, all the patients with mid-low rectal cancer and T1–3 at the preoperative staging may benefit from the down-to-up approach. Obviously, the transanal approach seems to achieve the best technical and oncological advantages in the subset of patients with a narrow pelvis and a low rectal cancer. Previous rectal surgery is a contraindication to the taTME approach. Previous radical prostatectomy is not an absolute contraindication to the taTME approach but the dissection on the anterior rectal

<table>
<thead>
<tr>
<th>Study (year)</th>
<th>Patients (n)</th>
<th>taTME</th>
<th>BMI kg/m²</th>
<th>Low rectal cancer (%)</th>
<th>Complete TME (%)</th>
<th>Nearly complete TME (%)</th>
<th>Incomplete TME (%)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kang et al. (2010)</td>
<td>340</td>
<td>No</td>
<td>24.1</td>
<td>NA</td>
<td>73.5</td>
<td>16.5</td>
<td>5.6</td>
<td>[2]</td>
</tr>
<tr>
<td>Van der Pas et al. (2013)</td>
<td>1044</td>
<td>No</td>
<td>26.1</td>
<td>17</td>
<td>88</td>
<td>9</td>
<td>3</td>
<td>[3]</td>
</tr>
<tr>
<td>Marinello et al. (2015)</td>
<td>625</td>
<td>No</td>
<td>NA</td>
<td>42</td>
<td>Low 72</td>
<td>Mid 83</td>
<td>Low 9.5</td>
<td>[17]</td>
</tr>
<tr>
<td>Helbach et al. (2015)</td>
<td>80</td>
<td>Yes</td>
<td>27.5</td>
<td>5.3 cm†</td>
<td>88</td>
<td>9</td>
<td>3</td>
<td>[14]</td>
</tr>
<tr>
<td>Lacy et al. (2015)</td>
<td>140</td>
<td>Yes</td>
<td>25.2</td>
<td>29.3</td>
<td>97.1</td>
<td>2.1</td>
<td>0.7</td>
<td>[15]</td>
</tr>
<tr>
<td>Tuech et al. (2015)</td>
<td>56</td>
<td>Yes</td>
<td>27</td>
<td>100</td>
<td>84</td>
<td>16</td>
<td>0</td>
<td>[18]</td>
</tr>
<tr>
<td>Our series (2015)</td>
<td>63</td>
<td>Yes</td>
<td>25.2</td>
<td>68</td>
<td>85</td>
<td>15</td>
<td>0</td>
<td>[13]</td>
</tr>
</tbody>
</table>

†Mean distance from the anal verge.

taTME: Transanal TME; TME: Total mesorectal excision.
plane should be conducted cautiously since the risk of finding adhesions between the bladder and the rectum.

**How transanal TME (technical points)**

Synchronous transanal and abdominal dissection is possible and has two main advantages: first of all it allows a better exposure of the rectum when the top and bottom dissection planes are reached. Second, the operating time can be reduced. However, two experienced staffs of surgeons and nurses are required to work together without hampering each other.

For most surgeons, the two-step approach is preferred. The up-to-down approach as a first step has the advantage of avoiding the CO₂ retroperitoneal pneumodissection and the possible colon distension due to inadequate purse-string suture. However, the down-to-up approach as a first step has the important advantage of defining immediately the cancer location, the resection margin and the type of operation (low anterior resection versus abdominoperineal resection). In our experience, the taTME approach is usually the first surgical step unless peritoneal carcinomatosis is suspected.

Transanal approach: The patients are placed in a lithotomy position with the right arm along the body and the thighs/legs abducted and slightly flexed. The first type of approach depends on the location of the cancer (low versus mid rectal cancer):

- Low rectal cancer: a Lone Star Retractor (CooperSurgical, Inc., CT, USA) is inserted. After cutting the anal mucosa just above the dentate line, a sleeve mucosectomy ± partial/total intersphincteric resection is performed toward the anorectal junction and the rectal wall is circumferentially transected at the level of the anorectal junction. After the dissection of the first 2 cm of the lower rectum, the anal mucosa is closed with a running suture and a single-port device is placed;

- Mid rectal cancer: the single-port device is positioned in the anal canal. A purse-string suture is placed through the rectal mucosa to tightly occlude the rectum distal to the lower edge of the cancer. A full-thickness rectal transection is performed.

After entering the peri-mesorectal space, the pelvic cavity is inflated with CO₂ to a pressure of 10–12 mmHg. The 5-mm laparoscope is introduced trough the upper trocar. The right and left inferior trocars are used to place the dissection device and the grasper or the suction-irrigation device. The mesorectum is circumferentially dissected from down to up toward the anatomical landmarks of a ‘good’ taTME: the sacral promontory posteriorly, the Pouch of Douglas anteriorly and the iliac vessels laterally. In the posterior plane, after sectioning the rectosacral fascia, the dissection follows the concavity of the sacrum. The anterior plane of dissection is conducted in front of or behind the Denonvillier’s fascia according to the rectal cancer position. In the lateral plane, particular attention must be paid to the inferior hypogastric plexus, keeping

<table>
<thead>
<tr>
<th>Study (year)</th>
<th>Patients (n)</th>
<th>taTME</th>
<th>pT3–4</th>
<th>DRM+ rate</th>
<th>CRM+ rate</th>
<th>CRM– (mm)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van der Pas et al. (2013)</td>
<td>243</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>13.2%</td>
<td>8</td>
<td>[3]</td>
</tr>
<tr>
<td>Leersum et al. (2014)</td>
<td>425</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>=10%</td>
<td>NA</td>
<td>[21]</td>
</tr>
<tr>
<td>Denoist et al. (2014)</td>
<td>50</td>
<td>No</td>
<td>82% (T4 0%)</td>
<td>8%</td>
<td>2%</td>
<td>5</td>
<td>[11]</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>Yes</td>
<td>80% (T4 4%) (p = 0.324)</td>
<td>18%</td>
<td>4%</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Marks et al. (2013)</td>
<td>106</td>
<td>Yes</td>
<td>36.3% (T4 0%)</td>
<td>1%</td>
<td>3.8%</td>
<td>NA</td>
<td>[10]</td>
</tr>
<tr>
<td>Tuch et al. (2015)</td>
<td>56</td>
<td>Yes</td>
<td>T3 79% T4 3.6%</td>
<td>NA</td>
<td>5.4%</td>
<td>8</td>
<td>[18]</td>
</tr>
<tr>
<td>Kanso et al. (2015)</td>
<td>34</td>
<td>No</td>
<td>46%</td>
<td>0%</td>
<td>9%</td>
<td>7</td>
<td>[20]</td>
</tr>
<tr>
<td></td>
<td>51</td>
<td>Yes</td>
<td>39% (p = 0.57)</td>
<td>8%</td>
<td>10% (p = 0.88)</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Our series (2015)</td>
<td>43</td>
<td>Yes</td>
<td>T3 23% T4 4.6%</td>
<td>0%</td>
<td>2.4%</td>
<td>11</td>
<td>[13]</td>
</tr>
</tbody>
</table>

**CRM+**: Positive circumferential resection margin at final pathology; **CRM– (mm)**: Distance in millimeters of the circumferential resection margin from the rectal cancer edge at final pathology; **DRM+**: Positive distal resection margin at final pathology; **NA**: Data not available; **taTME**: Transanal total mesorectal excision.
the dissection in close contact with the fascia of the mesorectum.

Abdominal approach: The patient is placed in the Trendelenburg and right lateral tilt position. By using a hybrid single-port technique (SILSTM Port above the umbilicus, 10-mm VersastepTM trocar in the right iliac fossa [Covidien, MA, USA]), once the inferior mesenteric vessels are tied and a complete mobilization of the mid-distal transverse colon, splenic flexure and descending sigmoid colon is performed, the peritoneum of the Douglas pouch is sectioned and the previous transanal plane of dissection is easily found. Whenever technically feasible and oncologically safe, a low inferior mesenteric artery ligation is performed. The specimen can be extracted transanally but we prefer to extract it transabdominally (through the site of the SILS Port location), since most of the patients have bulky mesorectum and narrow pelvis. The section point in the descending colon is decided after having checked the presence of an adequate arterial flow of the vessels running along the colon length (the marginal vessels are cut and the presence of an adequate arterial flow is checked). A hand-sewn anastomosis (lateroterminal when feasible) is performed for cancers located in the lower rectum. For cancers located in the mid rectum, a pursestring suture of the rectal stump by prolene 0 is performed and tied around the rod of the anvil. The EEA™ 33 circular stapler (4.8-mm staples; Covidien) is inserted through the anorectal ring, linked to the rod, and then fired. A loop ileostomy is performed when needed.

**Conclusion & future perspective**

After the introduction by Heald of the TME concept in rectal surgery, the down-to-up approach (taTME) is one of the most interesting and promising surgical innovations of the last years. Besides the similar results in terms of postoperative morbidity compared with the gold-standard up-to-down approach, there are increasing data suggesting that taTME seems to achieve higher rates of negative resection margins and good quality TME among patients undergoing low anterior resection for rectal cancer. Similar

<table>
<thead>
<tr>
<th>Study (year)</th>
<th>taTME</th>
<th>Mid–low RC rate</th>
<th>Patients (n)</th>
<th>Morbidity rate</th>
<th>AL rate</th>
<th>OS/median follow-up</th>
<th>Local recurrence rate</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jeong et al. (2014)</td>
<td>No</td>
<td>100%</td>
<td>170 (laparoscopic)</td>
<td>21.2%</td>
<td>1.2%</td>
<td>91.7%</td>
<td>2.6%</td>
<td>[23]</td>
</tr>
<tr>
<td>Law et al. (2004)</td>
<td>No</td>
<td>67%</td>
<td>622</td>
<td>23.6%</td>
<td>7.3%</td>
<td>66.5%/39.6 months</td>
<td>8.1%</td>
<td>[24]</td>
</tr>
<tr>
<td>Penninckx et al. (2013)</td>
<td>No</td>
<td>100%</td>
<td>762</td>
<td>31.8%</td>
<td>8.4%</td>
<td>80.8%/NA</td>
<td>NA</td>
<td>[25]</td>
</tr>
<tr>
<td>Van der Pas et al. (2013)</td>
<td>No</td>
<td>68%</td>
<td>1044</td>
<td>40%</td>
<td>12%</td>
<td>NA</td>
<td>NA</td>
<td>[13]</td>
</tr>
<tr>
<td>Park et al. (2011)</td>
<td>No</td>
<td>100%</td>
<td>130</td>
<td>13.1%</td>
<td>3.8%</td>
<td>86.6%/32.5 months</td>
<td>2.6%</td>
<td>[26]</td>
</tr>
<tr>
<td>Portier et al. (2007)</td>
<td>No</td>
<td>100%</td>
<td>278</td>
<td>NA</td>
<td>NA</td>
<td>83.8%/67 months</td>
<td>10.6%</td>
<td>[27]</td>
</tr>
<tr>
<td>Denost et al. (2014)</td>
<td>No</td>
<td>100%</td>
<td>50</td>
<td>44%</td>
<td>32%</td>
<td>10%</td>
<td>2% (p = 0.2)</td>
<td>NA</td>
</tr>
<tr>
<td>Fernandez-Hevia et al. (2014)</td>
<td>No</td>
<td>100%</td>
<td>37</td>
<td>51%</td>
<td>32%</td>
<td>11%</td>
<td>5% (p = 0.4)</td>
<td>NA</td>
</tr>
<tr>
<td>Kanso et al. (2015)</td>
<td>No</td>
<td>100%</td>
<td>34</td>
<td>47%</td>
<td>47%</td>
<td>18%</td>
<td>27% (p = 0.3)</td>
<td>100%</td>
</tr>
<tr>
<td>Marks et al. (2013)</td>
<td>Yes</td>
<td>100%</td>
<td>106</td>
<td>13.2%</td>
<td>2.8%</td>
<td>95%</td>
<td>2.8% (38.6 months)</td>
<td>[10]</td>
</tr>
<tr>
<td>Lacy et al. (2015)</td>
<td>Yes</td>
<td>79%</td>
<td>140</td>
<td>34%</td>
<td>8.6%</td>
<td>97%</td>
<td>2.1% (15 months)</td>
<td>[15]</td>
</tr>
<tr>
<td>Our series (2015)</td>
<td>Yes</td>
<td>68.3%</td>
<td>63</td>
<td>25%</td>
<td>9.5%</td>
<td>92%</td>
<td>4.8% (23 months)</td>
<td>[13]</td>
</tr>
</tbody>
</table>

*3 years.
AL: Anastomotic leak; NA: Not available; OS: Overall survival; RC: Rectal cancer; taTME: Transanal TME.
findings have been found in terms of local recurrence and overall survival rates but studies with larger cohort of patients and longer follow-up times are required. A multicenter international randomized trial (COLOR III) [32] comparing transanal TME versus conventional laparoscopic resection of mid-low rectal cancer will start soon [33]. Do we really need a randomized study to validate this new procedure? I believe the answer is yes but it is important to keep in mind that well-designed randomized clinical trials are expensive and time consuming, and sometime, unethical. Infact, there are no doubts that the gold-standard treatment of resectable colorectal liver metastases in 2015 is surgery but no randomized studies were ever performed to confirm it. Studies conducted from existing databases offer an alternative to randomized studies, making it possible to study outcomes in a faster and less expensive way. For this reason, I believe that the national taTME registries, in other words, the Italian taTME registry [34] and the England taTME Registry [35] which are collecting large cohort of data from many European centers, hopefully will be soon able to draw more definitive conclusions regarding the oncological safety of this new procedure.

### Financial & competing interests disclosure
The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

### References
Papers of special note have been highlighted as:
- of interest
- of considerable interest


14. The largest series of transanal total mesorectal excision (taTME) for low rectal cancer.


19. A recent and large series of rectal cancer approached from up-to-down.

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**PERSPECTIVE**

- Large cohort European study reporting on taTME.

- Large cohort European study reporting on taTME.
  - Randomized study of laparoscopic versus open up-to-down total mesorectal excision for mid-low rectal cancers after neoadjuvant radiotherapy.
  - TATME. www.tatme.net
  - Transanal-TME. https://tatme.medicaldata.eu