Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

Supplementary Appendix

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A Phase III Prospective Randomized Trial Comparing Laparoscopic–assisted Resection versus Open Resection of Rectal Cancer: ACOSOG Z6051 (Alliance)

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Supplemental B: Credentialing

Surgeons (46 surgeons from 35 institutions) were credentialed in both laparoscopic colectomy and proctectomy. Surgeons submitted an unedited LapR video for review as part of the requirement for participation. Submission of 20 operative reports for both OpR of RC and LapR of RC or other deep pelvic dissection was used by the credentialing committee to qualify participants. Surgeons who did not take part in the Clinical Outcomes of Surgical Therapy (COST) Trial for laparoscopic colectomy for cancer had to submit 20 operative reports of laparoscopic colectomy for colon cancer with pathology reports to document basic laparoscopic skills.[18,20] Surgeons who participated in the COST trial did not take part in the colon part of the credentialing. Relevant features of the operation demonstrated for credentialing are in the Interventions section.

Surgeons choosing to utilize robotic techniques for the LapR were required to be credentialed in the use of robotic technique for the pelvic TME. Surgeons submitted operative and pathology reports (which included a photo of the TME specimen) from ten cases of robotic rectal dissection and an unedited video of the technique. No surgeon was credentialed only for robotics.

Supplemental C: Trial Modification

The primary outcome for the trial was the adequacy of the surgical approach determined by three oncological parameters: negative distal margins (DM, >1 mm between the closest tumor to the cut edge of the tissue), negative circumferential radial margins(CRM, >1 mm between the deepest extent of tumor invasion into the mesorectal fat and the inked surface of the specimen), and "complete" TME specimen (smooth surface of mesorectal fascia with all fat contained in the enveloping fascia, to a level 5 cm below the tumor for tumor specific TME for upper RC, or the entire mesorectal envelope present for low RC) or "nearly complete" (the mesorectal envelope is intact except for defects no more than 5 mm deep with no loss of mesorectal fat). For primary analysis "complete" and "nearly complete" grades were considered together. All three of the parameters (DM, CRM, and TME quality) had to be achieved for the surgery to be considered a "success".

The protocol-specified DM was modified from >2 cm on permanent section (or >1 cm on frozen section) to >1 mm midway through the study by consensus of the steering committee and DSMB because new findings demonstrated the DM in patients receiving neoadjuvant chemoradiation therapy could be less.22-35 A potential unintended consequence of the original DM requirements was an increase in the number of patients who underwent APR and colostomy when a low rectal anastomosis would have been sufficient.

Classification of the TME specimen as "nearly complete" differs from the description of the intermediate "intra-mesorectal" level of the dissection plane as originally described by Quirke and colleagues.[4] The "intra-mesorectal" classification refers to a dissection within the fatty mesentery and failure to remove all of the fat of the mesentery in total. The "intra-mesorectal" classification would be considered "incomplete" in the current study. The "nearly complete" designation reflects small superficial tears or defects in the fascia of the rectum less than 5 mm deep without loss of fat content of the mesorectum. This designation reflects some extraction trauma or incision into, but no removal of,

the fascia or fat. Based on current evidence, the Steering and DSMB committees adopted “Complete” and “nearly complete” TME as adequate specimens.[36]

Supplemental D: Operative and Pathology Review

A 20% sample of intraoperative videos of the laparoscopic technique from the first 100 cases of LapR was randomly selected for review by steering committee members of technique as quality control and random audit. This review was reported to the ACOSOG Data and Safety Monitoring Board (DSMB) before continuing the study, without the need for further audit of technique.

Photos of every TME specimen were requested and reviewed for quality by a third party observer blinded to technique used. The photograph of the TME specimen was taken either in the pathology laboratory or the operating room, and grading of TME quality occurred. The inclusion of TME grading in the synoptic pathology report was mandated by the American College of Pathology during the study period.

Of the completed surgeries, 352 (76.4%) of the photos were received. Reasons for missing photos was either the photo was not taken or there where technical issues in which the photo was lost. 330 (93.8%) of the 352 photos were interpretable and were assessed for TME quality. TME findings were compared between site reported and the photo review. Agreement was found in 226 (80.6%) cases.

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