therapy was a requirement for all individuals in our study undergoing breast-conserving surgery, and those in whom it was omitted (n = 2390) were excluded from analysis.1 Although we agree that the register we used does not give full details on given radiotherapy, we are confident that we can discern local (ie, whole-breast after breast-conserving surgery or chest wall after mastectomy) from locoregional radiotherapy (including the above-local target but adding regional nodal fields).

In a 2021 publication from our group using the same Swedish national register, we individually scrutinized the medical records of 4294 patients undergoing breast-conserving surgery from 2010 to 2016 and found that dose and fractionation rarely differed from guideline recommendations.2 Hence we are confident that deviations from the standard dose (50 Gy, with an additional boost dose for those younger than 50 years) and fractionation (n = 25) were uncommon in our study. During the relevant years (2008-2017), partial breast irradiation was not used in Sweden. Thus, the present study does not and cannot make any assumptions regarding the advantages or disadvantages of partial breast irradiation, and we cannot underpin or contradict the statement by Lin and colleagues regarding the cosmetic benefits of such radiotherapy.

That is assuming that the term locoregional radiotherapy in their Letter indeed regards partial breast irradiation according to the Intraoperative Irradiation for Early Breast Cancer (ELIOT) trial and not true locoregional radiotherapy as defined above.

We do not agree with the authors’ reference to a Nature Reviews Cancer study by Follain et al.3 While Follain and colleagues discuss different patterns of interstitial and distant tumor cell migration, there is no mention of the specific case of breast-conserving surgery and no argumentation for the existence of in-transit tumor deposits within the breast, which should, in that case, limit the safety of conservative surgery. What is more important is that mounting evidence from large cohort studies including the present work shows significantly better results after less extensive breast surgery, thus contradicting the presence of disease-relevant in-transit metastases within the breast.4

The use of fluorescence-based sentinel lymph node detection after neoadjuvant chemotherapy, as quoted by Lin and colleagues, is an entirely different topic and cannot be addressed with our population of primarily operated individuals. However, it may be noted that available clinical evidence so far after isotope-based sentinel node biopsy alone following neoadjuvant chemotherapy shows surprisingly few recurrences, which does not suggest any urgency to search for new ways of identifying sentinel lymph nodes in addition to the development of targeting strategies.5 Instead, it is crucial to gather more real-life evidence on the oncologic outcome after currently used axillary surgical staging techniques, an aim that is, among others, addressed by the ongoing prospective EUBREAST-03 AXSANA trial.6

In summary, while we appreciate the discussion of the above hypotheses, we wish to stress that none of these are the subject of our work and therefore can neither be corroborated nor rejected based on our data.

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Generalizability of the Results and Concerns About Leakage Rates of the ICAN Trial

To the Editor The ICAN trial has provided level 1 evidence favoring intrathoracic anastomosis after a total or hybrid minimally invasive esophagectomy.1 We commend the authors on a robust study design for a purely surgical trial. The quality control of the surgical technique before participation and later during the trial is meticulous and may lay the standard for future surgical trials.

The trial shows better outcomes with intrathoracic anastomoses for distal esophageal and gastroesophageal junction tumors. However, only 9 patients (3.7%) with mid-esophageal tumors were recruited in the trial. In our opinion, generalizing the results to midesophageal tumors may not be accurate.

Achieving an adequate proximal margin in midesophageal tumors and performing an intrathoracic anastomosis may be challenging. Also, midesophageal tumors, especially squamous cell carcinomas, would have received neoadjuvant chemoradiation. Siting the anastomosis on an esophageal stump that has received close to 45 Gy of radiation may affect the leak rates.2

Another issue to be considered is tumors with involvement of superior mediastinal lymph nodes. Total mediastinal
Lymphadenectomy may affect the vascularity of the remnant esophagus and viability of the anastomosis. We humbly submit that although this trial has successfully proven the cause of intrathoracic anastomoses for distal esophageal and gastroesophageal junction tumors, it has not adequately considered the compromises required in tumors in the middle third of the esophagus. Hence, we suggest that intrathoracic anastomoses be performed with caution in tumors in the middle third of the esophagus, particularly those with superior mediastinal lymphadenopathy or those receiving neoadjuvant chemoradiation.

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To the Editor With interest we have read the randomized clinical trial by van Workum et al. In their article, the authors show a reduction in anastomotic leakage rate from 31.7% to 12.3% with the introduction of an intrathoracic anastomosis. They conclude that “intrathoracic, as opposed to cervical, anastomosis resulted in better outcome for patients treated with transthoracic MIE [minimally invasive esophagectomy] for midesophageal to distal esophageal or gastroesophageal junction cancer.” Although this study is well performed and the authors have to be congratulated, we cannot fully concur with the conclusion and future recommendations in their article.

The main point of concern is the unacceptable high leakage rate in the cervical anastomosis arm. Therefore, the strong improvement in this trial cannot be used as a plea for a broad implementation of transthoracic minimally invasive esophagectomy, nor is the difference in outcome a conclusive argument in favor of the intrathoracic anastomosis.

Surgical complications of esophageal resections are monitored yearly in the Netherlands by means of the Dutch Upper GI Cancer Audit. In our institution (Leiden University Medical Center, the Netherlands) in the past 10 years, the anastomotic leakage was 18 of 416 patients (4.3%) for cervical anastomosis of whom 10 needed a reintervention (data extracted from Dutch Upper GI Cancer Audit database). Recurrent nerve palsy was registered in 25 of 416 patients (6.0%). We believe that creation of the gastric conduit and the anastomotic technique plays the main role in this difference.

Any introduction of a new (technically demanding and expensive) surgical technique should be weighed against the best standard of care. We believe that apart from technical innovations, improvement of surgical outcome can also be achieved by ongoing education and improvement of standard surgical techniques. Site visits and proctoring should not be overlooked as means to improve individual patient outcome.

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In Reply With great interest we read the Letters from Nittala et al and de Steur et al, and we thank them for their thoughtful comments on our study.1

In the Letter by Nittala et al, the generalizability of the results of the ICAN trial to the subgroup of midesophageal tumors is questioned. For the ICAN trial, we believed it was important that we only included patients in which both types of anastomoses were oncologically feasible. This resulted in the exclusion of cancers situated above the level of the carina because some surgeons argue these tumors generally require a cervical anastomosis. Because of this, only a small subgroup of patients in our study had cancer in the middle third of the esophagus, and we agree this groups is by far too small to draw any robust conclusions for this subgroup. In addition, we agree that there are theoretical arguments to believe leakage rates may be different in this subgroup. In addition, we agree that there are theoretical arguments to believe leakage rates may be different in this subgroup, although the clinical relevance of (most of) these remain to be proven in robust studies. Future studies will be needed to elucidate whether intrathoracic anastomosis also yields superior results for the subgroup of cancers in the middle third of the esophagus.

In the Letter by de Steur et al, the high cervical anastomotic leakage rate is discussed. We congratulate the authors on a low cervical anastomotic leakage rate of 4.3%, which is much lower than the Dutch mean of 21.9%, as is reported in a previous study with Dutch Upper GI Cancer Audit registry data.2 Higher than mean cervical anastomotic leakage rates that correspond with ours have been found previously in Dutch randomized clinical trials,3,4 which may indicate that an inclusive definition and careful data registration could have contributed to a comprehensive and complete reporting of anastomotic leak rate. However, we acknowledge the large difference between single-center leak rates, such as...
those reported by de Steur et al, and the rate found in our multicenter study. In our view, these large differences in leak rates should be subject of further study, but we should remain cautious when interpreting results of single-center studies until these techniques have been tested in large high-quality trials. Finally, we fully agree that finding the most optimal surgical technique and consequently spreading knowledge and skills through training, proctoring, and quality-improvement programs will be extremely important in optimizing outcome for patients undergoing minimally invasive esophagectomy.

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CORRECTION

Error in Abstract and Methods: In the Original Investigation titled “Stepped Collaborative Care Targeting Posttraumatic Stress Disorder Symptoms and Comorbidity for US Trauma Care Systems: A Randomized Clinical Trial,”1 published in the May 2021 issue, there was a repeated error in the Abstract and the Methods. In each place, the study end date given as “November 2018” should have been “November 2019.” This article has been corrected. This article was also corrected on March 31, 2021, to fix the spelling of an author affiliation.


Incorrect Term in Results: In the Original Investigation titled “Sex Differences in the Pattern of Patient Referrals to Male and Female Surgeons,”1 published in the November 10, 2021, issue of JAMA Surgery,1 an incorrect term was used in the Referral Homophily subsection of the Results section. The third paragraph’s first sentence should have ended with physicians instead of surgeons. The full sentence should read as follows: “Post hoc exploratory analysis limited to only those referrals associated with diagnostic codes related to breast issues suggested inbreeding homophily among female physicians, whereby female surgeons accounted for 26.0% of surgeons seeing patients with breast issues but received 30.7% of referrals from female physicians.” This article was corrected online.


Error in Text: The Viewpoint titled “Regional Variation in Surgical Procedure Rates: Going Beyond Description,”1 published on November 3, 2021, was corrected to fix an incorrect word in the sentence: “The presence of regional variation in surgical rates raises questions about the underlying causes, including whether the variation exceeds differences that could be expected due to differences in the prevalence of the underlying disease in the population, and whether physicians or patients are the primary drivers of trends.” The word “traits” should have been “rates.” This article was corrected online.


Error in Author’s Name: In the Original Investigation titled “Challenging Traditional Paradigms in Posttraumatic Pulmonary Thromboembolism,”1 published online December 15, 2021, there was a spelling error in an author name. The spelling of the 10th author “Elliott R. Haut, MD,” should have been “Elliott R. Haut, MD.” This article was corrected online.