preserving the main part of segment 8 is not labeled correctly anatomically as a left hepatic trisectionectomy (H123458-B, according to the NEW WORLD terminology[2]) but should be labeled as an extended left hemihepatectomy (H123458'-B-MHV or H12345'8'-B-MHV[2]). Thus, I would like to stress that this parenchyma-sparing procedure should not be included in the category of a left hepatic trisectionectomy. The notation in my paper, "According to my experience with more than 200 left trisectionectomies for PHC, the number of bile ducts to be anastomosed is usually only 1 or 2, occasionally 3, very rarely 4, and never 5 or more,"[1] is correct in the case of H123458-B. In addition, the authors stated that "the conclusion that left hepatic trisectionectomy can safely be performed in experienced hands is therefore ambiguous." However, this conclusion statement was not found at all in my article. Anyway, if my word choice troubled the authors, I sincerely apologize for my somewhat exaggerated description.

Left-sided hepatectomy preserving the main part of segment 8 may be indicated in some cases of perihilar cholangiocarcinoma with left-sided predominance, although thus far I have rarely performed such a procedure. In this parenchyma-sparing procedure, the right posterior bile duct is divided at the level of the right anterior portal vein because this vein must be preserved. This bile duct resection line is the same as that offered by left hemihepatectomy (H1234-B[2]) and more distal (hilar side), ~7 mm distal (hilar side) according to my previous study,[3] compared to the resection line offered by left hepatic trisectionectomy. This shorter proximal ductal margin in the parenchyma-sparing procedure leads to an increased incidence of R1 resection with a positive proximal ductal margin.[3] Importantly, when the confluence of the right anterior and posterior bile ducts is involved in perihilar cholangiocarcinoma with left-sided predominance, left hepatic trisectionectomy, not a parenchyma-sparing procedure, should be selected principally if the hepatic function is stable to achieve R0 resection.[1,3]

Masato Nagino, MD, PhD✉
Department of Gastroenterological Surgery, Aichi Cancer Center Nagoya Japan.
✉ m.nagino@aichi-cc.jp

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Response to the Comments of Onerup et al and Lu and Song on: "Effects of Community-based Exercise Prehabilitation for Patients Scheduled for Colorectal Surgery With High Risk for Postoperative Complications: Results of a Randomized Clinical Trial"

Reply:

We read with interest the recently published comments of Onerup et al[1] and Lu and Song[2] on our randomized controlled trial.[3] We thank the authors for their valuable comments. Prehabilitation programs have been shown to improve physical fitness before hospitalization and surgery. However, evidence that this consequently also reduces postoperative complications still seems inconclusive and opposing.[4] The systematic review of Thomas et al[4] states that prehabilitation of patients before hospitalization and surgery for major intra-abdominal cancer seems to improve postoperative outcomes when specifically focused on adequately identified high-risk surgical patients. Onerup et al[5] recently performed an randomized controlled trial with 761 patients to evaluate the effect of a short-term, unsupervised home-based physical exercise intervention before and after colorectal cancer surgery on self-assessed physical recovery. All eligible patients greater than or equal to 20 years of age planned for elective colorectal cancer surgery were included. No effect from their perioperative physical exercise intervention on short-term self-reported physical recovery was found. Carli et al[6] demonstrated that prehabilitation by (pre)frail patients, selected with help of the Fried frailty index that combines 2 short performance items with 3 self-reported items, preparing for resection of colorectal cancer did not reduce the incidence of postoperative complications. Although they intended to include less physically fit (prefrail and frail) patients undergoing colorectal cancer resection, an alternative strategy might be more appropriate to select those patients that truly require prehabilitation. Patients with low preoperative aerobic fitness would be expected to benefit the most from prehabilitation. Therefore, identification and—in the context of clinical a trial—selection of high-risk patients based on cardiopulmonary exercise testing (CPET) might be the risk assessment strategy of choice. When performing CPET is not possible, more practical performance-based field tests might be useful for preoperative risk assessment. The steep ramp test (SRT), a short-time maximal test on a cycle ergometer, might be a suitable alternative as SRT performance is strongly related to aerobic fitness. Moreover, lower SRT performance is associated with postoperative morbidity in colorectal cancer surgery.[7] As Lu and Song[2] suggested, the 6-minute walk test, though being a submaximal field test and therefore less correlated with aerobic fitness, might be an alternative strategy. Nevertheless, further validation is required for both the SRT and 6-minute walk test.[8]

Onerup et al[1] stated that our supervised community-based physical exercise intervention could only be performed by <5% of the total population with colorectal cancer screened and assessed during our study period, which limits the generalizability of the results. We think this statement is not correct, since we specifically aimed at identifying and including patients at high risk for postoperative complications, based on a predefined CPET criterion, and to evaluate the effectiveness of an exercise prehabilitation program in this specific group, and not in the total population of patients with colorectal cancer. Consequently, in line with what Onerup et al[1] stated we focused statements concerning generalizability purely on this specific subpopulation, while the moderate participation rate of 56% among high-risk patients who were eligible should be kept in mind. When preoperative screening for potential modifiable risk factors is incorporated in the perioperative care pathway as part of usual care, Van Wijk et al[9] recently showed in their study that all of the 100 screened patients with

hepatobiliary and pancreatic cancer participated in preoperative risk assessment.

One of our inclusion criteria was the willingness to perform community-based prehabilitation at a physical therapy practice in the catchment area of both hospitals. Onerup et al[1] stated that this information should have led to several participants suspecting the nature of the intervention and included a selection of study participants. However, since we informed patients in the prehabilitation group and the usual care group differently, patients in the usual care group did not receive information about the possible effects of prehabilitation. These patients received a patient information letter about the registration of perioperative data and the hypothesized relation of aerobic fitness with postoperative complications after colorectal resection. Therefore, the aforementioned inclusion criteria (willingness to perform community-based prehabilitation) only applied to patients randomized to the prehabilitation group. Moreover, patients in the usual care group were planned for surgery at the earliest convenience. This resulted in a mean (SD) time between inclusion and surgery of 34.6 (28.8) days in the prehabilitation group versus 19.0 (10.2) days in the usual care group ($P < 0.001$).

As Onerup et al[1] and Lu and Song[2] properly declare, there is a small, nonsignificant, difference in the number of smoking patients in the prehabilitation group (n = 1, 4%) and usual care group (n = 6, 21%, $P = 0.112$) and in the number of patients with an age-adjusted Charlson Comorbidity Index of 6+ in the prehabilitation group (n = 4, 14%) and usual care group (n = 7, 24%, $P = 0.416$). Smoking was not associated with postoperative complications, as there were 3 smoking patients without complications and 4 smoking patients with complications ($P = 1.00$). Onerup et al[1] questioned whether there could have been any bias in the final allocation of the participants with participants with unhealthy lifestyle habits and comorbidity dropping out between randomization and the final intention to treat population. Of the 39 patients allocated to the prehabilitation group, 11 patients were excluded from the final intention-to-treat analyses. Of these 11 patients, only 1 patient with an unhealthy lifestyle was excluded because he withdrew from surgery. The remaining 10 patients were excluded for other reasons, not related to unhealthy lifestyle habits (eg, adequate preoperative aerobic fitness, complete remission after neoadjuvant therapy). Based on these figures, we are convinced that the small differences in smoking and age-adjusted Charlson Comorbidity Index between the groups not affected the allocation and dropout.

Our study was specifically and exclusively powered to detect a statistically significant difference in the number of patients with 1 or more postoperative complications between the prehabilitation group and usual care group.[3] We agree with Onerup et al[1] that especially the prevention of severe complications would be of great relevance to the patients, caregivers, the need of health care resources, and, consequently, costs. However, costs associated with the prevention of (the impact of) complications would probably outweigh the costs of the care for the postoperative complications, and preventing complications (also minor complications) would considerably reduce the patient's physical, mental, and social burden. In The Netherlands, it was shown that the average total hospital costs (primary admission and after discharge up to 90 days) for a patient without complications is ~€9000 versus ~€11,500 and ~€27,000 for a patient with minor and severe complications, respectively.[10] The estimated costs of a *multi*modal prehabilitation program are €969 per patient (containing 12 supervised physical therapy sessions, protein supplements, project management, and data collection).[11] Moreover, the results of our study showed that the total hospital costs of patients in the prehabilitation group were €1300 lower than of patients in the usual care group (to be published). We, therefore, expect prehabilitation to be a cost-effective ingredient of the care of high-risk patients undergoing colorectal surgery and suggest implementing the interventions according to what was shown to be successful in our paper. On top of that, we recommend, while implementing, to evaluate the cost-effectiveness in the context of each unique hospital and its catchment area.

In future research, multidisciplinary preoperative risk assessment in multiple domains should be performed to identify patients at higher risk of an impaired postoperative outcome.[12] Preferably, the identified modifiable risk factors should be optimized before surgery. Future prehabilitation trials should focus on the adequate selection of high-risk surgical patients (ie, patients with a low preoperative aerobic fitness based on evidence-based cutoff values of field tests), and should provide personalized, multimodal, and (partly) supervised high intensity prehabilitation programs at home or in a community-based setting with objectively monitoring a patient's progression.[3] To support patient adherence to the program and empowerment for self-management, remote monitoring (ie, physical activity, physiological signs, and patient-reported outcomes and experience measures) might be useful, as Lu and Song[2] suggested, but needs to be proven in proper experimental trials. Moreover, to reach all patients, we would advise to have prehabilitation considered in every hospital and/or clinical guideline as usual care in high-risk patients scheduled for elective colorectal surgery.

Annefleur E.M. Berkel, MD, PhD
Department of Surgery, Medisch Spectrum Twente, Enschede, The Netherlands.

Bart C. Bongers, MSc, PhDbart.bongers@maastrichtuniversity.nl
Department of Nutrition and Movement Sciences, School of Nutrition and Translational Research in Metabolism (NUTRIM), Faculty of Health, Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands

Nico L.U. van Meeteren, PhD
Department of Anesthesiology, Erasmus Medical Center, Rotterdam, The Netherlands

Joost M. Klaase, MD, PhD✉
Division of Hepato-Pancreato-Biliary Surgery and Liver Transplantation, Department of Surgery, University Medical Center Groningen, Groningen, The Netherlands
j.m.klaase@umcg.nl

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