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Research paper

Ultra low-dose chest ct with iterative reconstructions as an alternative to conventional chest x-ray prior to heart surgery (CRICKET study): Rationale and design of a multicenter randomized trial

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ABSTRACT

Background: Stroke after cardiac surgery is a severe complication with a persistently high incidence of 1.4 – 9.7%. Postoperative strokes are mainly embolic and can be provoked by manipulation and clamping of the aorta during cardiac surgery, resulting in the mobilization of atherothrombotic material and calcifications from the aortic wall. Computed tomography (CT) can offer preoperative visualization of aortic calcifications with low radiation exposure. We hypothesize that preoperative knowledge regarding the location and extent of aortic calcifications can be used to optimize surgical strategy and decrease postoperative stroke rate.

Methods/design: The CRICKET study (ultra low-dose chest CT with iterative reconstructions as an alternative to conventional chest x-ray prior to heart surgery) is a prospective multicenter randomized clinical trial to evaluate whether non-contrast chest CT before cardiac surgery can decrease postoperative stroke rate by optimizing surgical strategy. Patients scheduled to undergo cardiac surgery aged 18 years and older are eligible for inclusion. Exclusion criteria are pregnancy, a chest/cardiac CT in the past three months, emergency surgery, concomitant or prior participation in a study with ionizing radiation and unwillingness to be informed about incidental findings. Subjects (n = 1.724) are randomized between routine care, including a chest x-ray, or routine care with an additional low dose chest CT. The primary objective is to investigate whether the postoperative in-hospital stroke rate is reduced in the CT arm compared to the routine care arm of the randomized trial. The secondary outcome measures are altered surgical approach based on CT findings and cost-effectiveness.

1. Introduction

Postoperative stroke is a major complication in 1.4 – 9.7% of patients undergoing cardiac surgery.[1] Stroke rates strongly depend on the surgical procedure, with higher rates for valve surgery, especially when combined with coronary artery bypass grafting (CABG). Stroke is associated with high postoperative mortality and a longer period of hospitalization.[2] A recent editorial highlights the fact that the incidence of stroke after isolated CABG, the most commonly performed cardiac surgical procedure, has not decreased over the past 10 years and occurs in 2.2% of patients.[3] Although various interventions and modifications of the surgical technique have been developed, randomized trials to demonstrate

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their benefit are lacking. This is partly due to the relatively low incidence of stroke which makes it more difficult to perform adequately powered trials. Postoperative strokes are mainly embolic in nature and often provoked by intraoperative manipulation of the aortic root and ascending aorta, which can result in mobilization of atherothrombotic material and calcifications from the aortic wall.[1,4] During surgery, the ascending aorta is clamped to initiate cardiopulmonary bypass. Patients with atherosclerosis of the ascending aorta have an almost five-fold higher risk of developing a postoperative stroke.[5] Although intraoperative manual palpation can be used to detect aortic atherosclerosis, it has only modest reliability.[6] Intraoperative direct epiaortic ultrasound is a valuable tool, but has a limited anatomical coverage and is operator dependent.[7] Furthermore, direct intraoperative ultrasound is only possible after sternotomy has been performed. This is a major drawback as it would be preferable to have detailed knowledge about aortic anatomy prior to surgery. In patients with extensive aortic calcifications this may even lead to the choice of alternative therapies because operative risk may outweigh benefits.

Unenhanced computed tomography (CT) can offer preoperative visualization of aortic calcifications as a marker of ascending aortic atherosclerosis. CT provides a 3D dataset with a high spatial resolution and offers the possibility to preoperatively plan surgical strategy. Recent technical innovations, including iterative reconstruction, allow a low radiation dose.[8] Several small, non-randomized studies indicate that a preoperative CT in cardiac surgery can possibly reduce postoperative stroke rate by adapting surgical strategy to avoid manipulation of the atherosclerotic aorta.[9]

The CRICKET study (ultra low-dose chest CT with iterative reconstructions as an alternative to conventional chest x-ray prior to heart surgery) has been developed to investigate whether a management strategy that includes preoperative chest CT compared to routine preoperative chest x-ray can reduce the stroke rate after cardiac surgery. Furthermore, this study investigates the cost-effectiveness and cost-utility since a CT is associated with higher costs compared to chest radiography. Here, we describe the rationale and design of this multicenter randomized controlled clinical trial (RCT).

2. Methods

2.1. Overall study design and participants

The CRICKET study is a prospective, multicenter randomized clinical trial (RCT) to investigate whether preoperative chest CT in patients scheduled for cardiac surgery can lower postoperative stroke rate by optimizing surgical strategy compared to standard chest x-ray. The study is registered at www.clinicaltrials.gov (NCT02173470). All sites currently participating in this study are academic medical centers in Europe. Patient inclusion started in September 2014 and is expected to be completed in 2018.

Patients scheduled to undergo cardiac surgery aged 18 years and older are eligible for inclusion. Exclusion criteria are pregnancy, a chest or cardiac CT in the past three months, emergency surgery, concomitant or previous participation in a study that exposed the patient to radiation and unwillingness to be informed about incidental findings on the CT scan such as lung nodules and vertebral fractures (Table 1). Patients scheduled for transcathether aortic valve implantation (TAVI) are not eligible for inclusion, because these patients routinely receive preoperative contrast-enhanced CT.

2.2. Study objectives

The primary study objective is to investigate if information about aortic calcifications derived from preoperative unenhanced low dose CT of the chest can lower in-hospital stroke rate after cardiac surgery by optimizing surgical strategy. The secondary objectives are (1) to investigate change in surgical approach, based on information derived from the preoperative chest CT, and (2) to assess the cost-effectiveness and cost-utility of the strategy that includes chest CT compared to routine care from a societal perspective.

2.3. Ethical considerations

The institutional review board of the University Medical Center Utrecht reviewed and approved the study protocol (NL47293.041.13). Furthermore, the radiation safety committee and executive board of each center approved the study. The risk due to radiation was estimated to be low to intermediate according to the ICRP guideline Radiological Protection in Biomedical Research.[10] Subjects will only be included in the study after written informed consent is provided. Four centers are currently participating in this trial: University Medical Center Utrecht, Maastricht University Medical Center, Erasmus Medical Center Rotterdam (all located in The Netherlands) and the Heart and Vascular Center of Semmelweis University, Budapest, Hungary.

2.4. Sample size calculation

Pilot data based on the largest and most comprehensive study reported in literature suggest that a 4-fold reduction in stroke rate (from 3.0% to 0.7%) is possible in patients undergoing a CT before cardiac surgery.[11] The local incidence of postoperative stroke was 1.9% in 2010 in University Medical Center Utrecht. Since this is relatively low compared to the literature, a slightly higher expected stroke rate of 2.0% was used for sample size calculation. Given a 0.05 type-1 error and a 0.80 type-2 error, 1.724 patients are necessary to detect a reduction in stroke rate from 2.0% to 0.5%. Patients that withdraw consent before the CT scan is performed will be replaced by new patients to reach the required number of included patients. Patients that withdraw from study participation after the CT scan is performed will not be replaced.

2.5. Patient recruitment and randomization

All patients eligible for inclusion are asked by a physician, physician-assistant or nurse(-practitioner) to participate in the trial when they visit the hospital for preoperative tests. After signing informed consent, patients are randomized using a web-based randomization procedure. Patients are randomized on a 1:1 basis to either the control or intervention group. The control group receives routine care including a preoperative chest x-ray. The patients in the intervention group receive an additional low-dose non contrast-enhanced chest CT scan the day before surgery (Fig. 1). Randomization is performed in blocks of eight in which the number of patients in the control and intervention group are divided equally. Randomization is stratified per center.

2.6. CT protocol

All CT acquisitions are performed with state-of-the-art multidetector row CT (MDCT) systems (64-slice or higher). No contrast agent is administered. Tube voltage is 80 KV and tube current (mAs) is set as low as possible to achieve effective radiation doses below 1 mSv for all acquisition settings. Images are reconstructed with