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RESEARCH LETTER

Initiation of the Scandinavian Trial of Uncomplicated Aortic Dissection Therapy

Kevin Mani [a], Timothy Resch [b], Beate Rikken Lindberg [c], Patrick Björkman [d], Oscar David Rubio [e], Jacob Budtz-Lilly [f,*]

[a] Department of Surgical Sciences, Section of Vascular Surgery, University of Uppsala, Uppsala, Sweden
[b] Department of Vascular Surgery, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark
[c] Department of Cardiothoracic Surgery, Rikshospitalet, Oslo University Hospital, Oslo, Norway
[d] Department of Vascular Surgery, Helsinki University Hospital, Abdominal Centre, Helsinki, Finland
[e] Department of Vascular Surgery, Landspitali University Hospital, Reykjavik, Iceland
[f] Division of Vascular Surgery, Department of Cardiovascular Surgery, Aarhus University Hospital, Aarhus, Denmark

The class and level of evidence from the European Society for Vascular Surgery (ESVS) guidelines regarding the care of patients with clinically uncomplicated type B aortic dissection (uTBAD) reflect the extant literature;[1] that is, medical therapy is requisite and early thoracic endovascular aortic repair (TEVAR) can be considered. Because of this, or perhaps in spite of this, variation in treatment strategies prevails and a randomised controlled trial is needed.[2,3]

The Scandinavian trial of Uncomplicated Aortic Dissection Therapy (SUNDAY Trial) is a pragmatic randomised controlled trial designed to answer the question whether a strategy of early TEVAR improves five year survival. All 22 major aortic centres in the five Nordic countries collaborated in its initiation in 2023. Subjects with uTBAD are randomised at least one week after symptom onset to either standard medical therapy alone or standard medical therapy + TEVAR. If allocated to TEVAR, this must be performed within 90 days from the onset of symptoms. This reflects the reported subacute window of treatment, where balance is maintained between favourable aortic remodelling and acceptable operative risks.[4] The primary endpoint is overall survival at five years. Secondary endpoints include aortic related death, re-interventions, neurological events, quality of life (QoL), costs, and survival at 10 years. The QoL surveys include the EuroQOL-5D-5L, the Hospital Anxiety and Depression Score (HADS), and the 12 item Short Form Survey (SF-12). Sample size calculations call for inclusion of 554 subjects, based on the hazard ratio of 0.52 identified from the Investigation of Stent Grafts in Aortic Dissection extended (INSTEAD-XL) trial and powered at 80%.[5] While the full protocol has previously been published, a notable recent amendment was approved to extend the inclusion window to 90 days.[6] Ethical approval has been obtained in all participating countries. The inclusion and exclusion criteria are detailed in Table 1.

Importantly, the designation of uncomplicated is a clinical one, such that anatomical or technical eligibility constraints do not impact inclusion, nor do anatomical or clinical high risk features. This point touches on the important trait of pragmatism to the trial. Any scrutiny of these patients, their anatomy, and aptitude of the vascular surgery team reveals a diversity of views regarding technical and clinical appropriateness. Within the trial, for patients randomised to TEVAR the method of surgical intervention is performed as per the treating unit's preference, with adjunctive procedures as deemed necessary. Thus, all options are available regarding various procedures, such as possible left subclavian revascularisation or distal aortic treatment extension, and used at the treating physicians' discretion.

There are other important nuances to this trial that, again, are pragmatic yet indispensable. Firstly, the medical

Table 1. Inclusion and exclusion criteria for subject enrolment in the Scandinavian trial of Uncomplicated Aortic Dissection Therapy (SUNDAY Trial).

Inclusion criteria
All subjects, aged ≥18 years at the time of informed consent signature, admitted or referred to the participating cardiovascular sites with uTBAD of <90 days duration.
Exclusion criteria
Subjects with no signed informed consent.
Subjects presenting with complicated type B aortic dissection.
Subjects previously treated in their descending aorta, either open surgery or TEVAR.
Subjects with pre-existing thoraco-abdominal aortic aneurysm.
Subjects with other aortic pathology with an indication for intervention that requires TEVAR.
Subjects with traumatic aortic dissection.
Subjects with an established connective tissue disease at the time of randomisation, including but not limited to Marfan's and Loeys–Dietz syndrome.
Subjects with a clinically estimated life expectancy <2 years.
Subjects with dementia.
Subjects who are pregnant or nursing.
Subjects with current sepsis.
Subjects currently participating in other clinical interventional trials.

uTBAD = uncomplicated type B aortic dissection; TEVAR = thoracic endovascular aortic repair.

* Corresponding author. Division of Vascular Surgery, Department of Cardiovascular Surgery, Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, 8200 Aarhus, Denmark.
E-mail address: jacoblilly@clin.au.dk; (Jacob Budtz-Lilly).
@BudtzJacob

therapy is considered and denoted standard as opposed to optimal or best, as no guidelines or consulted medical experts consider one regimen as optimal or best, and local protocols are used. All subjects, however, are equipped with home blood pressure apparatus, and values from their logbooks as well as data on medical treatment will be recorded for analysis and evaluation of confounding. Secondly, there are no diagnostic imaging related outcomes (e.g., aortic remodelling), although limited morphological measurements are recorded for sub-analytical purposes. Thirdly, follow up data are recorded at three months and one, three, and five years, as well as any re-admissions. In other words, once randomisation has taken place, sites can maintain their local imaging, clinical follow up, and rehabilitation protocols. The only requisite data at follow up include living status, blood pressure readings, and QoL forms.

The possible vulnerability of pragmatism, given the limited exclusion criteria and, in particular, lack of anatomical exclusions, is the maintenance of equipoise and the risk of crossover. Fundamentally, however, the generalisability of the results should be upheld, as will the preservation of prognostic balance when applying the intention to treat analysis. Similar healthcare models and strategies of treatment in the Nordics should favour balanced recruitment, and an expert committee has been created in order to help sites in decisions regarding inclusion. Importantly, the primary endpoint of the trial (five year survival) is universally captured within Nordic countries through national registries, reducing the risk of loss to follow up for the primary endpoint in the trial. To date, 28 patients have been included from 15 initiated sites over nine months. Given the above stated sample size of 554 patients, the uTBAD incidence and population estimates in Scandinavia suggest an accrual period of approximately four years.

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