Review Article

Downstream thoracic endovascular aortic repair following the frozen elephant trunk procedure

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Abstract: The frozen elephant trunk technique has become a well-established treatment option for patients presenting all thoracic aortic pathologies including acute and chronic dissection, aortic aneurysms and even penetrating aortic ulcers involving the aortic arch and descending aorta. Nevertheless, there is a significant incidence of and risk for distal aortic reinterventions after the frozen elephant trunk. Indications mainly include a planned staged approach, diameter progression of downstream aortic segments and the development of distal stent-graft induced new entries (dSINEs). Endovascular stent-graft extension through conventional thoracic endovascular aortic repair (TEVAR) is a relatively simple and safe method to address any pathologies in the remaining descending thoracic aorta up to the level of the coeliac trunk. In fact, the frozen elephant trunk stent-graft provides an ideal proximal landing zone for any endovascular stent-graft extension. Postoperative outcomes are very promising with very low reported in-hospital mortality and morbidity. In case this 2-staged-approach fails to stabilize the remaining aorta, a 3-step procedure, namely open thoracoabdominal aortic replacement, is simplified because the anastomosis site has moved distally. Follow-up of all patients, following frozen elephant trunk implantation or distal stent-graft extension, is mandatory, ideally in an outpatient clinic dedicated to the aorta in order to identify disease progression or to detect any complications as soon as possible.

Keywords: Aorta; frozen elephant trunk; distal stent graft-induced new entries (dSINEs); stent graft; aortic clinic

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Introduction

The frozen elephant trunk procedure has significantly enriched the therapeutic armamentarium for aortic arch aneurysms, acute or chronic aortic dissections (type A, type non-A-non-B or type B), and even for patients with penetrating aortic ulcers involving the aortic arch (1-9). European societies recommend the frozen elephant trunk procedure over isolated aortic arch replacement or the conventional elephant trunk because of the excellent artificial proximal landing zone the frozen elephant trunk stent graft provides and its capability to expand the true lumen and/or to close proximal entries within the descending aorta (10). Frozen elephant trunk technique is furthermore the preferred method for aortic arch replacement because it is an anticipatory strategy aiming to prevent the underlying aortic pathology's potential progression in the downstream segment (4,10,11).

The increasing use of frozen elephant trunk has been accompanied by two distinct surgical developments: first,

there is a trend towards a more proximal surgical aortic arch anastomosis (zone 1 or 2 rather than zone 3) to simplify the surgical procedure (8,10,12). Second, shorter stent-graft lengths are liberally employed to enhance spinal cord protection (8,13,14). Both trends cause proximalization of the frozen elephant trunk stent graft close to or within the aortic arch. The stent graft therefore covers less downstream aorta, and may fail to align with the aorta's natural orientation and instead, create a sharp angle between the stent graft and downstream aorta. This could cause pathological flow patterns towards the aortic wall, but more importantly, possibly raise the risk for dissection membrane perforations (14). These distal stent graft-induced new entries (dSINEs) have been identified as a significant clinical problem following the frozen elephant trunk procedure (14-16).

Aortic reinterventions following the frozen elephant trunk procedure

Despite the fact that the frozen elephant trunk procedure was originally intended as a single-step intervention, there is growing evidence of a significant risk for aortic reinterventions after the frozen elephant trunk procedure (8,17). Our group has already analyzed the risk for aortic reinterventions via competing risk regression analyses (competing risk: death), and we managed to quantify the risk for secondary aortic interventions to as high as 64% after 3 years (17). Importantly, this risk incorporates planned or expected secondary aortic reinterventions as well as truly unexpected or unplanned interventions.

There are usually three clinical scenarios in which the frozen elephant trunk stent graft may be the first step in a dichotomous treatment strategy because of the ideal platform for secondary aortic interventions. First, younger patients obviously carry an inherent risk for secondary aortic interventions following any kind of aortic repair because of their comparably longer life expectancy and higher likelihood of underlying connective tissue diseases. Hence, in younger patients, where detrimental aortic remodeling of downstream aortic segments seems likely, frozen elephant trunk treatment may be an effective surgical option. Second, the frozen elephant trunk device may be used in patients to manage any aortic pathology within the ascending aorta, the aortic arch and/or the proximal descending aorta in whom additional pathologies in the descending aorta are present but where the threshold for downstream thoracic aortic interventions has not yet been reached. Third, the frozen elephant trunk procedure may be the treatment of choice, but the stent-graft component may not be long enough to address an additional aortic pathology within the proximal to mid-descending aorta. One possible clinical example is an aortic dissection with a large communication in the proximal descending thoracic aorta that is a few centimeters distally too far for the frozen elephant trunk stent graft.

For these conceptual, planned, or expected secondary aortic reinterventions following the frozen elephant trunk, the "risk" designation seems inappropriate and the indication for the aortic reintervention is usually considered the aorta's expanding diameter. Yet there is growing evidence of the considerable likelihood of unintended and unexpected aortic reinterventions following frozen elephant trunk treatment (8,13,14,16,18).

dSINEs are known to be one major cause of unintended reinterventions following the frozen elephant trunk procedure (13,14,16,17). This term describes a new entry caused by a stent graft's distal end regardless of the natural disease progression or iatrogenic injury; dSINEs cause perfusion of the false lumen and are associated with a considerable risk for negative aortic remodeling potentially triggering acute aortic rupture (19,20). Therefore, a dSINE diagnosis should be considered as treatment failure, because mortality rates for untreated dSINE are known to be as high as 25% (20). Importantly, we previously reported on the risk of dSINE development of up to 25% 3 years after the frozen elephant trunk procedure, and that dSINE may develop at any time after frozen elephant trunk implantation (14,15). In fact, dSINE usually develop asymptomatically and are frequently diagnosed in routine follow-up computed tomography angiography scans. While no specific risk factors were identified in recent studies, it seems plausible that the proximalization of the frozen elephant trunk stent graft and a potentially sharper angle between the frozen elephant trunk stent graft and native true lumen orientation may be associated with dSINE development (14). Hence, the advantages of a zone 2 implantation (better surgical exposure) and the use of shorter stent grafts (spinal cord protection) need to be weighed against the risk for dSINE development (8,13,14,21).

Another major cause for unintended aortic reinterventions is the development of endoleaks usually associated with the underlying aortic pathology's progression (17). In addition, reports are emerging of thrombi being diagnosed within the frozen elephant trunk stent graft during the

Table 1 Overview of current literature of downstream endovascular repair following the frozen elephant trunk procedure

Author, year	N	In-hospital mortality	Permanent SCI	Stroke
Kreibich *et al.*, 2021 (13)	66	0	0	0
Loschi *et al.*, 2021 (26)	20	1	1	0
Meisenbacher *et al.*, 2021 (30)	20	1	1	2
Haensig *et al.*, 2020 (28)	10[#]	1	0	0
Pan *et al.*, 2017 (29)	23	0	0	0
Laranjeira Santos *et al.*, 2017 (27)	8	1*	0	0

[#], including 2 patients treated using the PETTICOAT technique; *, patient expired within 30 days following TEVAR—in-hospital status unclear from publication. SCI, spinal cord injury; PETTICOAT, provisional extension to induce complete attachment; TEVAR, thoracic endovascular aortic repair.

early postoperative period that may also require an urgent intervention (17,22).

Reinterventions

Open surgery with a conventional open anastomosis to the stent-graft portion of the frozen elephant trunk has been done early with acceptable in-hospital results (23). However, the open approach requires prolonged left lung compression and is associated with significant morbidity (17,23). Moreover, there is evidence of massive intraoperative bleeding through the stent-graft portion and postoperative stent-graft damage (24,25). The exact causes remain unclear, but it has been suggested that stent-graft clamping may cause damage to the graft itself or that a stent graft's unfolding/stretching may result in loss of neoadventitia or neointima in the straightened graft and consequently cause bleeding through multiple micropores (24,25).

Therefore, many centers follow an endovascular approach by carrying distal stent-graft extension out as the distal treatment of choice (13,26-30). Through this approach it is possible to extend down to the level of the thoraco-abdominal transition, that is, to the level of the coeliac trunk, observing very good postoperative outcomes (*Table 1*). Taking this approach, any remaining disease can also be transformed into a Crawford-Type 4 pathology and simplify significantly any necessary third-step intervention (31). In fact, it seems reasonable that patients benefit through this "3-step-approach" because of shorter operative times for open thoracoabdominal aortic replacement, and the left lung's ventilation and/or compression need not be interrupted during surgery. The latter is a key aspect in improving postoperative outcome in these patients (31).

Technical aspects of downstream thoracic endovascular aortic repair (TEVAR)

In accordance with current European consensus statements, TEVAR extensions are usually performed in our hybrid operating room by a cardiovascular resident supervised by a board-certified cardiovascular surgeon (32). As part of our integrated open surgical and endovascular training, we believe that endovascular skills are paramount for aortic surgeons and patient outcomes are not compromised by our training approach (33).

The day before TEVAR distal stent-graft extension, we routinely implant cerebrospinal fluid (CSF) drainage to maximize spinal cord protection—one of our primary concerns when treating the descending aorta: this is the reason why we generally avoid performing concomitant frozen elephant trunk surgery and stent-graft extension. Rather, we attempt downstream TEVAR at least 14 days following a frozen elephant trunk implantation, preferably even longer, because of the collateral network development. Intra- and postoperatively, we monitor the patient continuously and, when necessary, regulate CSF pressure. We also routinely take other spinal cord protection approaches including elevating the arterial blood pressure, assuring an adequate hemoglobin level, fast-track concepts and serial postoperative neurological examination. Drainages are usually removed 24 hours postoperatively (34). Note that a clear consensus on the prophylactic use of CSF drainages is still missing (32).

Today, we almost exclusively execute our endovascular interventions percutaneously via pre-closure techniques (Proglide, Abbott Medical, Chicago, IL, USA). We land proximally within the frozen elephant trunk stent graft and usually oversize by 2 mm (most proximal stent-graft

diameter to the stent-graft diameter of the Thoraflex hybrid prosthesis). In most cases, we use the whole 10 cm length of the frozen elephant trunk stent-graft as a proximal landing zone to avoid any endoleak type 1a. In case of classical aneurysm formation, we aim for 10% oversizing at the distal landing zone; in case of chronic dissections, we routinely use tapered stent grafts and size the distal end according to institutional standards to avoid oversizing (13,14,35).

Outcomes after stent-graft extension

Current literature reveals excellent in-hospital results following downstream endovascular repair following the frozen elephant trunk procedure with very low incidences of permanent spinal cord injury (SCI), stroke, or death (*Table 1*).

Conclusions

There is a significant incidence of and a risk for distal aortic reinterventions following frozen elephant trunk implantation. Extending the stent graft via conventional TEVAR is a relatively simple and safe method to address pathologies in the remaining descending thoracic aorta up to the level of the coeliac trunk. Postoperative outcomes are very good with no reported in-hospital mortality. If this 2-stage-approach fails to stabilize the remaining aorta, a 3-step procedure, namely open thoracoabdominal aortic replacement, is made simpler because the anastomosis site has moved distally.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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