Descemet membrane endothelial keratoplasty: graft rejection, failure and survival

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CHAPTER 4

Refining the Terminology of Graft Failure in Reports of Endothelial Keratoplasty Outcomes

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VIEWPOINT

Graft survival studies are important to evaluate the longevity of transplanted donor corneal tissue. Since 1998, corneal transplantation has undergone an evolution from conventional techniques such as penetrating keratoplasty to minimally invasive techniques such as Descemet stripping (automated) endothelial keratoplasty, and Descemet membrane endothelial keratoplasty for the treatment of corneal endothelial diseases.[1]

To assess the "graft survival" rate in a cohort of patients, the eyes that developed irreversible corneal edema for "endothelial graft failure" need to be determined. In the literature on penetrating keratoplasty, the terms *primary* and *secondary graft failure* are used to describe early endothelial failure (primary: cornea did not clear after surgery) as a result of endothelial damage during surgery and late endothelial failure (secondary: cornea cleared initially but showed decompensation at a later time point) resulting from endothelial decay owing to postsurgical inflammation, allograft rejection, suture-related inflammation, or glaucoma (surgery), among other things.[2] Therefore, *graft failure* and *graft survival* may have been used as mirroring terms pointing in opposite directions; both terms reflect the "graft success rate" in terms of endothelial survival, either from a positive angle (survival) or a negative angle (failure). In other words, in the penetrating keratoplasty literature, "graft failure" equaled "endothelial failure" and indirectly reflected the graft survival rate in a cohort. As a result, "graft survival" became synonymous with "endothelial survival".

In endothelial keratoplasty, these definitions may no longer be interchangeable for 2 reasons *(Figure)*. First, owing to the techniques available, the endothelium may be functional but simply not able to function depending on the attachment status of the Descemet membrane endothelial keratoplasty graft. As an extreme example, in an eye with a completely detached graft floating in the recipient's anterior chamber, the graft may be perceived as having "failed" because the cornea is edematous, but a detached graft has also been shown to carry a viable and potent endothelium, but no corneal clearance can be anticipated owing to its anatomically false position.[3] The same holds for eyes with a graft positioned "upside down," where the cornea is also most often edematous owing to a detached and anatomically false oriented graft (endothelium facing recipient stroma). Referring to such grafts as having failed is a rather colloquial term used for a "clinically or technically unsuccessful" graft, but it is misleading in terms of actual endothelial survival. It may be important in an eye with corneal edema

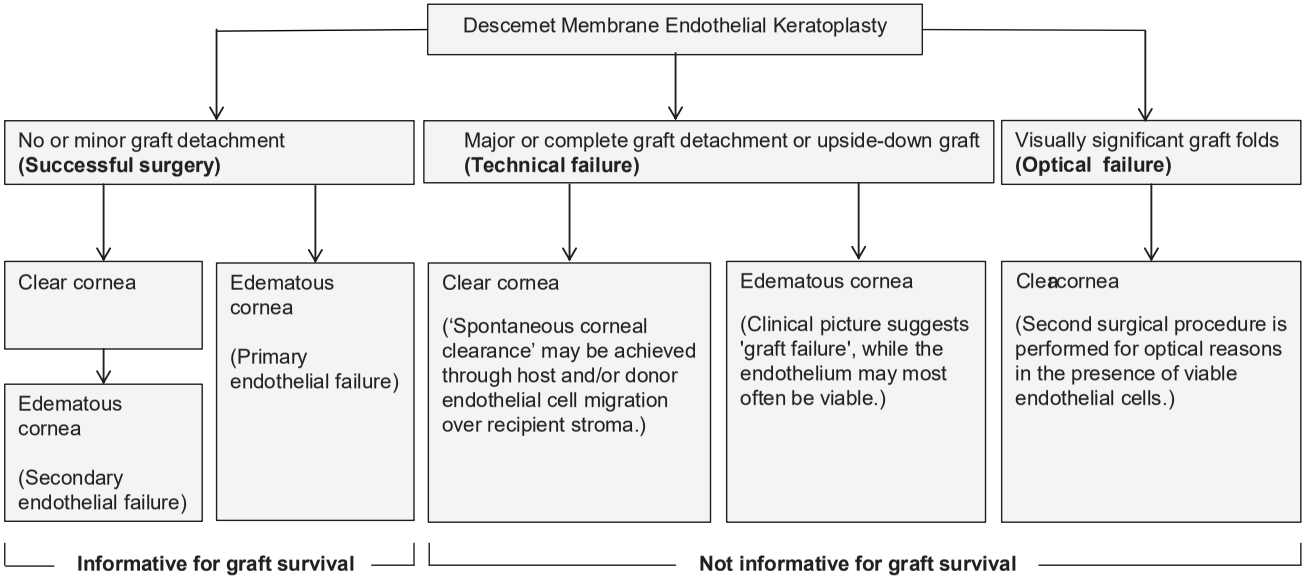

Figure. Schematic representation of the relationship between graft attachment status and endothelial viability (i.e., graft survival).

after Descemet membrane endothelial keratoplasty to differentiate between a "technical failure" and a real endothelial dysfunction because after complete apposition by a rebubbling procedure or after correct orientation, these grafts frequently show good viability (i.e., corneal deturgescence and clearing). Clearly, a graft cannot "fail" and be viable at the same time. Therefore, the definition for "graft failure" and "graft survival" should be reconsidered for endothelial keratoplasty studies.

The second reason for fine-tuning definitions is that the currently used terms may also be misleading the other way around in endothelial keratoplasty. In cases with a partial or complete graft detachment after Descemet membrane endothelial keratoplasty, the cornea may also show "spontaneous corneal clearance."[4] Hence, in these cases, the cornea may also clear despite the graft dehiscence, requiring no further surgical intervention. Naming this condition, a graft failure (because of the graft detachment) also seems to be a misnomer, especially when considering that, in these eyes, the endothelial cell density measurements may reflect endothelial cell migration (from the donor and/or recipient) over the recipient's posterior stroma, which means that these cases may also show a different long-term endothelial cell survival than grafts with complete apposition.[5]

Similarly, despite a clear cornea with a functional endothelium after Descemet stripping (automated) endothelial keratoplasty, visual rehabilitation may be limited by graft folds or interface scarring. Referring to these grafts as "failed" rather than "optically unsuccessful" seems to be a misnomer as well.[6] The same applies to penetrating keratoplasty when replaced for other reasons than endothelial failure[7] (e.g., unsatisfactory refractive outcomes). Not only from a surgical and clinical point of view but also considering the efficacy of eye banking, "graft survival" should only refer to (donor) endothelial cell survival, and these evaluations should not be diluted with false-positive ("spontaneous corneal clearance") and false-negative (surgically unsuccessful) cases.

In our opinion, therefore, the terminology used for graft survival studies needs to be further refined because the term graft failure is no longer synonymous with endothelial failure and, therefore, has become less informative (e.g., completely detached endothelial graft carrying viable endothelium) and because the term graft success rate does not mimic graft viability (e.g., spontaneous clearance after host endothelial cell migration). To enable the comparison of future corneal transplant survival studies, it would seem more accurate to evaluate graft attachment status, corneal clearance status, and the presence of visually significant

graft folds when a second surgical procedure is indicated to distinguish actual "endothelial graft failure" from "technical failure" and "optical failure" (Figure).

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