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MATCH
Management of Post-Transplant Infections in Collaborating Hospitals

Classification of Death Causes after Transplantation (CLASS): Evaluation of Methodology and Initial Results

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BACKGROUND

- Correct classification of underlying causes of death is an important component of conducting interventional research to improve quality of care in transplant medicine.
- Temporal surveillance of changes in the patterns of underlying causes of deaths among transplant recipients is required to detect potential emerging health threatening challenges in this vulnerable patient population[1,2,3,4].

AIMS

- To develop and validate a method to reliably classify underlying causes of death in hematopoietic stem cell (HSCT) and solid organ (SOT) transplant recipients and to identify characteristics that could identify deaths with a clear cause.

METHODS

- The methodology included case record form (CRF) registration, a central adjudication process, and a recorded underlying cause of death (**Figure 1**).
- Characteristics associated with agreement of the underlying "recorded cause of death" between 2 external reviewers (independent agreement) and between the investigator-designated and the recorded cause of death were determined using Cohen's Kappa statistics (95% CI).
- The method was derived on patients who died 2010-2013 and validated on patients who died 2013-2016 in the MATCH cohort (consecutive patients transplanted at a large tertiary transplant centre in Copenhagen).
- The recorded underlying cause of death using the methodology was compared to underlying cause of death in the Danish National Death Cause Registry (DNDCR).

RESULTS

- 388 transplant recipients died during 2010 to 2016 (286 (74%) and 102 (26%) in derivation and validation cohort, resp.).
- 196 (51%) SOT and 192 (49%) HSCT.
- Leading underlying recorded causes of death among SOT and HSCT were cancer (20%, 48%), graft rejection/failure/graft-vs.-host-disease (35%, 28%), and infections (20%, 11%), resp. Distribution of recorded cause of death according to cohort is shown in **Table 1**.

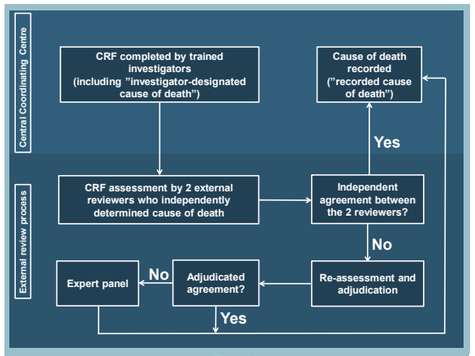


Figure 1
Assessment process of the CLASS project.
CRFs were completed by trained investigators at the Central Coordinating Centre. CRFs include clinical information around the time of death. Furthermore, the investigators proposed a cause of death (investigator-designated cause of death). The completed CRFs were then sent to 2 external reviewers who each independently determined cause of death. If the reviewers achieved independent agreement of the cause of death, the case was finalized and cause of death recorded. In case of disagreement, the case was re-assessed and adjudicated. Upon agreement, the adjudicated cause of death was recorded . In case of continuing disagreement, the cause of death was decided by an expert panel.

Table 1
Distribution of recorded cause of death (determined by the external reviewers after adjudication or an expert panel) in derivation and validation cohort

Recorded cause of death	All cases N (%)	Derivation Cohort N (%)	Validation Cohort N (%)
Cancer	133 (34)	96 (34)	37 (36)
Graft rejection/GvHD/ Graft failure	120 (31)	88 (31)	32 (31)
Infection	61 (16)	46 (16)	15 (15)
Organ failure or dysfunction	37 (10)	25 (9)	12 (12)
Cardiac or vascular disease	23 (6)	20 (7)	3 (3)
Other causes	2 (0)	2 (1)	0 (0)
Unknown	12 (3)	9 (3)	3 (3)
Total	388 (100)	286 (100)	102 (100)

RESULTS (CONT.)

- Kappa of independent agreement between the 2 external reviewers was 0.64 (0.56-0.69) in the derivation cohort and 0.63 (0.52 – 0.73) in the validation cohort.
- Kappa between the investigator-designated and the recorded cause of death was 0.74 (0.69-0.80); comparable in the validation cohort. Kappa was highest among those where cause of death was recorded as cancer (**Figure 2).**
- In both cohorts, Kappa of agreement between the investigator-designated and the recorded cause of death was "substantial" among recipients with "no history of liver disease AND no history of cerebrovascular disease" (information retrieved from the CRF); κ=0.78 (0.72-0.84) and κ=0.74 (0.64-0.84) in the derivation (N=206) and validation cohort (N=75), resp.
- The underlying cause of death recorded in the CLASS project was concordant with the DNDCR in 37% and 38% in the derivation and validation cohort, resp. (**Figure 3**).

SUMMARY

- We developed and validated a method (entitled CLASS) to systematically and reliably classify cause of death among transplant recipients.
- There was a high degree of agreement of underlying cause of death between the investigator-designated and the recorded cause of death (determined by the external reviewers after adjudication or an expert panel).
- Cause of death (recorded cause) of recipients without a history of liver disease and cerebrovascular disease was correctly classified by investigators in most cases suggesting that these are deaths with a clear cause, which therefore may not require external reviewer assessment.
- There was a high degree of discordance between this classification and that in the national death registry. Studies and surveillance using data from these registries may be unreliable and therefore may misguide the health challenges that transplant recipients are faced with.

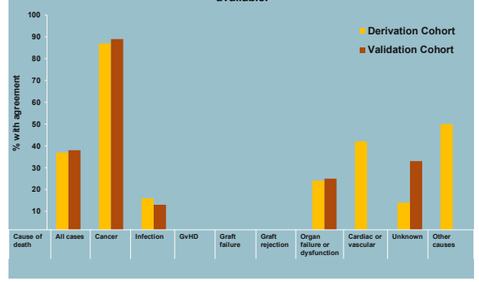
CONCLUSIONS

- This is the first validated method to reliably classify underlying cause of death in transplant recipients. The method can be applied to any cohort. Electronic support structures to handle the process depicted in **Figure 1** is available as part of a collaborative platform.

Figure 2
Agreement (% and Kappa) between investigator-designated cause of death (proposed in CRF) and the recorded cause of death (determined by the external reviewers after adjudication or an expert panel) according to recorded cause of death in derivation and validation cohort

*Other causes (N=2) and Unknown causes (N=12) not included in the figure due to few numbers.

Figure 3
Agreement between recorded cause of death (determined by the external reviewers after adjudication or an expert panel) in the CLASS project and the National Death Cause Registry among those (N=376) where this information was available.



References:
1. Pascual M et al, N Engl J Med 2002
2. Johnston SD, Transplantation 2002
3. Christie JD, J Heart Lung Transplant 2011
4. Kahwaji J, Transplantation 2011

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