Agreement between health care claims and the physician's follow-up visits in the determination of post-transplant immunosuppressive therapies: the CESIT study

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Background

Maintenance immunosuppressive therapy, indicated for patients after solid organ transplantation – kidney (R), liver (F), heart (C), lung (P) – and aimed at preventing rejection, involves the intake of at least one Calcineurin (CNI) inhibitor (Cyclosporin – CsA – or Tacrolimus – TAC) in combination with an Antimetabolite (Antim) (Mycophenolate Mofetil or Mycophenolic Acid – MMF – or Azathioprine – AZA) or a proliferation signal inhibitor (mTOR) (Sirolimus – SIR – or Everolimus – EVE) with the possible addition of corticosteroids (in particular Prednisone – PRED). The possibility of comparing prescribing patterns identified through different data sources represents an important methodological challenge and could shed light on the accuracy, advantages, and limitations of different information sources, aspects that must be considered when planning future observational studies.

Objectives

To assess, within a cohort of solid organ transplant patients, the levels of concordance in the definition of post-transplant immunosuppressive therapy between health administrative flows and what is reported by the medical specialist during the patient's periodic follow-up visit.

Design

Analysis of the level of concordance of information on post-transplant maintenance immunosuppressive therapy collected from two different data sources: the regional health administrative databases (SIS) and the national transplant information system (SIT). This analysis was performed as part of a retrospective cohort study – the CESIT study – including all patients undergoing single solid organ transplantation (heart, liver, lung, kidney) between 2009 and 2019 in four Italian regions (Lombardy, Lazio, Veneto, Sardinia). The therapeutic combinations of immunosuppressants were identified by means of specific algorithms applied to the SIS data and subsequently compared with the therapeutic patterns recorded by specialist physicians during follow-up visits (FU) and entered electronically in the SIT flow sheets. The analysis focuses mainly on the therapy delivered in the 30 days following hospital discharge (index therapy); it is then extended to comparisons made over longer time windows (at 1, 2, and 3 years from the date of hospital discharge).

Main outcome measures

The level of agreement between the two data sources in defining the index therapy was assessed using three methods: 1. Cohen's k statistic: this method allowed quantification of the level of agreement at the level of individual active substance; 2. proportion of active ingredients in common: an ordinal categorical variable was calculated for each patient indicating the level of concordance between the sources: null (no active ingredient in common), low (<40 % of ATCs in common), medium (40-59 %), high (>60 %), perfect (identical combinations); 3. Levenshtein distance (LS): considering polypharmacies from a formal point of view as strings, the computational effort that would be required to make them equal was estimated.

Results

There were 2,692 solid organ transplant patients for whom index therapy information was available from both SIS and SIT (C: 6.8%; F: 44.9%; P: 5.2%; R: 43.1%). In comparison to CNI immunosuppressants, Cohen's k coefficient showed high levels of concordance for all transplant types (CsA heart: 0.78; CsA liver: 0.96 – TAC heart: 0.74; TAC kidney: 0.92); while for MMF, differential performance by organ type was evident (MMF heart: 0.51; MMF kidney: 0.78). For the Preds, there was greater discordance in particular in R and F. When comparing immunosuppressive therapy as a whole, the 'high/perfect' concordance levels concerned on

average 80.1% of the patients (F: 70.1%; R: 91.3%). The results were comparable by applying LS. Finally, the concordance at 1, 2, and 3 years after discharge reported a less good performance than with index therapy, which was, however, stable over the time intervals considered.

Conclusions
The level of concordance between therapeutic combinations for the same patient detected between different sources was generally high: despite this, the level of agreement varied according to the individual active substance, the type of transplant and the time window examined. The results of this work show that SIS are a valuable tool for defining immunosuppressive maintenance therapies and offer useful elements to consider when planning observational studies based on the two data flows.