

Results of a Literature Review to Prepare Data Modelling in the Context of Kidney Transplant Rejection Diagnosis

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Abstract. Due to demographic change the number of serious kidney diseases and thus required transplantations will increase. The increased demand for donor organs and a decreasing supply of these organs underline the necessity for effective early rejection diagnostic measures to improve the lifetime of transplants. Expert systems might improve rejection diagnostics but for the development of such systems data models are needed that encompass the relevant information to enable optimal data aggregation and evaluation. Results of a literature review concerning published data models and information systems concerned with kidney transplant rejection diagnostic lead to a set of data elements even if no papers could be identified that publish data models explicitly.

Keywords. kidney, graft rejection, transplant, decision support, data warehouse, data model, literature review, diagnosis

1. Introduction

An increase in severe kidney disease and, as a result, an increasing need for kidney transplants (NTx) can be expected due to demographic change. Compared to this increasing demand, there is a shortage of available donor organs at the same time [1]. Therefore, the early detection of graft loss reactions in kidney transplants is of great importance, not at least for this reason. According to [2], acute cellular rejection reactions occur in 30% of the cases in the first year after NTx and in up to 70% or 80% of the cases during the entire course of treatment. In the ERDF²-funded joint project "Screen-Reject: A lateral flow test for rejection diagnostics" a new diagnostic tool is being developed to improve and fasten the diagnosis of graft rejection [3]. Participating partners of the joint project are the Technical Chemistry of the Leibniz University, the Institute of Transfusion Medicine of the Hanover Medical School and the University of Applied Sciences and Arts of Hanover.

In the sub-project "Screen-Reject: Clinical data warehouse for graft rejection diagnostics according to NTx" of the collaborative project, the Hannover University of

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Applied Sciences and Arts is developing a Data Warehouse (DWH), which will serve as a starting point for the development of an expert system to support the graft rejection diagnosis based on clinical data. In order to provide a starting point for the development of the DWH, a literature review was conducted to provide an overview of expert and information systems and their supporting data structures in the context of kidney transplantation and graft rejection diagnostics. The aim of the research is to identify, categorize and synoptically summarize relevant systems, data models and data fields. The outcome of the literature review ought to be extended by expert interviews, to ensure the quality of the results and support the development of a data model for kidney graft loss diagnostic.

2. Materials and methods

The literature review bases on the literature database PubMed. For the development of the search query, a preliminary inquiry was developed, which led to a recall of 2318 scientific papers. The screening of the results revealed that many of the identified papers are dealing with the results of epidemiological analyzes based on national epidemiological registers. In a second step an optimization of the search query resulted in a recall of 166 papers. The abstracts of publications found were analyzed and then subjected to a full-text analysis. Based on these results a representation overview of relevant contents was generated.

The search query was built by constructing blocks of relevant keywords describing relevant topics. As depicted in table 1 three blocks could be identified by connecting informatics, medical and medical/technical topics. Each block was filled by combining several keywords with wildcards, nesting and OR-statements. The blocks were combined with AND-statements to finally perform the literature retrieval.

Table 1. Topics used in block construction for information retrieval.

block	keywords
informatics	Data Model, Data Warehouse, Decision Support System, Database
medical	kidney, nephrology, renal, renal transplantation
technical	transplant

A classification accompanied the analysis of the 166 abstracts, where five inclusion criteria were used. The leading inclusion criteria was the occurrence of the topic 'renal disease', which was combined with four technical terms. The classification as content about 'Data model', 'Databases/Register in NTx-topic', 'Data Warehousing' and 'Decision Support Systems' was used to identify relevant papers for full-text analysis. The year of publication was not used as an exclusion criterion due to the assumption of a small number of publications on this particular subject.

130 papers were excluded after analysis of the abstract because they did not cover any technical issues or describe dedicated data used. 36 paper were included for full text analysis to acquire further information about relevant data structure and information systems. Subsequently, the papers were categorized based on their content.

A mind map was generated depicting the data fields found that were used in graft rejection diagnosis (Figure 1). For every data field found in the literature a branch of the mind map was added. Due to continual information gained from the literature analysis, the fields were constantly rearranged in a suitable order.

3. Results

36 works were identified as relevant through full-text analysis. Twelve of these papers deal with clinical decision support systems. Three publications mention DWH technologies. Eight papers dealt with the evaluation of national registries with regard to graft loss and graft survival. Twelve papers dealt with databases on specific NTx-related issues, such as immunosuppression or organ vs. recipient databases. One single publication was concerned with new primary diagnoses in the nephrological field. None of the publications describes data models or data structures in the context of NTx diagnostics of graft loss.

Even if no publications concerning specific data models could be identified some conclusions about relevant data fields could be drawn supported by the identified literature: In addition to the usual patient demographics, recipient data (e.g. creatinine values), data fields concerning donor information (e.g. diseases, living / deceased), transplant specific data (e.g. cold ischemia time), immunosuppression data, diagnostic data, virologic and transplant immunological data such as HLA information or ABO incompatibility could be identified as relevant for rejection diagnostics.

The generated mind map provides a synopsis of the complex of required graft rejection related data in addition to related publications in this field of research (figure 1). Knowledge of databases and registries in nephrologic research and the promoting organizations was systematically documented.

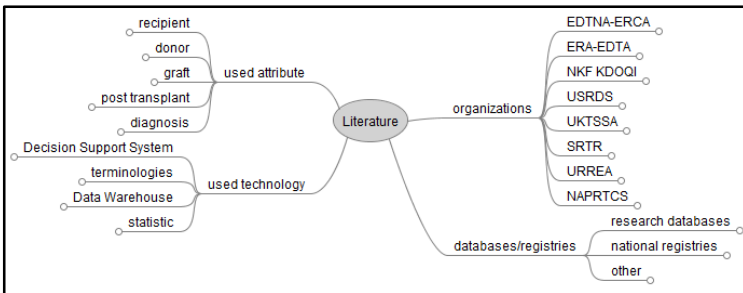


Figure 1. Information by literature - mind map.

A mind map (Figure 1) presents a list of references to scientific work: For each attribute addressed in research, a list of references to scientific papers has been created. Table 2 presents an excerpt of the attributes found and the amount of references.

Table 2. (Excerpt) Attributes found in literature with quantities of references. Shown is the highest amount of references for each characteristic. There were a total of 40 attributes with 125 verifiable references.

Entity	Attribute	Number of verifiable literature
recipient	age	6
graft	HLA	9
donor	virology	6
diagnosis	principal diagnosis	9
post transplant examination	immunosuppression	11
Total number	40	125

In total 40 main characteristic features were found by 125 literature references in the full text analysis, which can be assigned to 5 entities (table 3). In independent expert interviews, 23 main characteristic properties were identified. All the characteristics

mentioned by the clinical experts were found, sometimes in modified form, in the literature. Some of the characteristics listed in the literature could not be identified as relevant by the clinical partners. A total of 32 out of 40 main characteristics found in the literature were identified as relevant. Fields such as "race", "height/weight" and "body mass index" for donor and recipient were not required by clinical experts.

Table 3. Entities found in literature with quantity of characteristics for each.

Entities found in literature	Total quantity of characteristics	Literature references per entity
recipient	14	32
graft	10	35
donor	9	24
diagnosis	4	17
post-transplant examination	3	17
count	40	125

Twelve papers dealing with decision support systems have also been identified. The papers are dealing with different topics in the field of decision-supporting procedures. It was possible to identify three topics which the papers deal with. Six papers were identified that deal with different topics in the field of drugs for the treatment of kidney transplants, such as immunosuppression, drug interaction in kidney specific treatments or general drugs in the treatment of kidney transplants, e.g., [4].

Three papers concentrate on the research areas referred to as "organ supply" are describing the reaction of transplant and recipient or the best genetic combination for donor and recipient, e.g., [5].

Three papers were summarized under the term "other post-Tx", which are dealing with the chances of survival after transplantation, nursing following transplantation and infections following transplantation. [6].

4. Discussion

Currently several projects focus on the research field of information system support for NTx follow-up care. For example, "NTx 360°" deals with the support of patient care according to NTx through a portal for patients, doctors and laboratories using telemedicine methods [7]. "ROCKET", which started on 01.09.2018, aims at improving the functional life of kidney transplants and will contribute to individual diagnosis, prognosis and risk stratification through web-based applications [8]. "Certain Registry" is a pediatric kidney transplant registry of the Society for Pediatric Nephrology and has been used for clinical studies since 2011 [9]. "TBase2" is a web-based electronic patient file that collects all treatment-relevant data from kidney patients [10,11].

Despite the fact that different corresponding projects are known, the results of the literature review indicate that no data models have yet been published in the context of NTx graft rejection diagnostics. The literature found deals with NTx issues such as the support in finding the optimal combination of graft and recipient or the support in the medication of organ recipients. But the identified systems are not focusing explicitly on expert systems for renal graft rejection diagnostics. Information needed to model specific data models for this question can be derived from existing literature, but should be mapped and compiled specifically. The development and publication of data models for this specific question can provide added value for this topic.

The results of this review can be used as a basis for further development and data modelling and combined with findings from expert interviews. The requirements

concerning such a data model raised by local clinical experts were synchronized with the literature identified by the review: The clinical experts considered 32 of the 40 attributes mentioned in the papers as being relevant for a data model. These results show that literature research can help developing a data model for renal rejection diagnostics.

Furthermore, initial information research in machine learning and decision support technology for kidney transplant rejection diagnosis could be initiated to facilitate the development of a clinical expert system for this application field.

One weakness of this study is the precision of its results, because many of the work found is concerned with statistical modelling and does not address data modelling per se. Thus not all of the papers found are listed in the references below³.

For future work, it would be an improvement if data models in this and other clinical research areas are published in a freely accessible way to enable experts to discuss their ability to cover the relevant information for specific application fields. This kind of clinical data model governance would reduce the efforts of software development in this field. Furthermore, the publication of such models, e.g. as openEHR templates in the Clinical Knowledge Manager (CKM), can be seen as an option for our research.

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³ more papers were identified; please contact the author for a complete list