Prioritization of Organ Transplant Patients using Analytic Network Process

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Abstract
Necessity of accurate prioritization according to clinical status and appropriate allocation of donor which balance medical urgency, efficiency, transplant benefit and equity is undeniable in order to minimize mortality rate of patients who wait for transplantation. This paper proposes a multi criteria decision making model using Analytic Network Process (ANP) approach to prioritize patients on Transplant Waiting Lists (TWL). In the first step, criteria/sub criteria which play role in prioritizing patients on TWL have been identified by reviewing the research literature. Main criteria considered here are urgency, efficiency, benefit and equity. Considering the relations between these criteria, a network with 4 criteria and 18 sub-criteria have been proposed. In the next step ANP method is adopted to prioritize patients on TWL. The proposed model overcomes the limitations of previous works by integrating views of many organ allocation approaches, improving the decision maker’s ability to collaborate, and by considering the feedbacks and interfaces. Our computational study suggests that the proposed model remains robust under various criteria weight change scenarios. We conclude that the insights from this model improves decision makers’ confidence in the organ allocation procedure, increase quality of life and usefulness of the organ, and more importantly decrease mortality rate and enhances welfare to society.

Key words

1. Introduction
Transplantation medicine is a complex, multi-faceted area, requiring the involvement of many specialist teams. The ultimate goal is to improve the length and quality of life in a patient with an irreversible terminal disease [2]. Liver transplant is the best option for end-stage liver disease. But currently there is a great difference between the number of needed organs and the available ones for transplantation and approximately, 18 people die each day waiting for an organ transplant [1]. Transplant communities’ major challenge is to try to develop strategies to close this gap between the number of patients in need of a transplant and the available organs [4]. Since resources are limited, the greatest challenges are prioritizing patients, exploring ways to enhance the donor pool and maximizing the outcome from available organs [2]. Optimal prioritization of the transplant candidate waiting list and appropriate allocation of organs could both reduce mortality of patients waiting for transplantation and prevent futile operations [1]. The Organ Procurement and Transplantation Network (OPTN) operates per a federal regulatory framework known as the Final Rule [22]. The Final Rule demands the OPTN to ‘increase and ensure the effectiveness, efficiency and equity of organ sharing in the national system of organ allocation’ and to ‘increase the supply of donated organs available for transplantation’ [1, 22].

In this study we try to use the criteria and sub-criteria relevant for organ transplant recipient selection which were identified based on literature and discussion with medical staff in order to build a comprehensive model. This paper proposes a Multi Criteria Decision Making (MCDM) framework to prioritize patients on waiting lists for transplantation according to different clusters of criteria. Current literature focuses on either qualitative or quantitative discussion, and few papers address the combination of both types when developing a model. In this study we combine tangible and intangible factors in order to propose a general and practical methodology. We use a MCDM model using Analytic Network Process (ANP) approach to prioritize patients on Transplant Waiting Lists (TWL). By creating a balance between urgency, efficiency, benefit and equity and by considering the feedback and interfaces within (inner
dependence) and between (outer dependence) clusters of elements (criteria) an ANP model provides a feasible alternative to existing models. The use of the ANP makes the model more accurate, easy to implement, easy to use and easy to update if necessary. This type of problem is critical and important because the generation of a preferred outcome in a timely manner could make the difference between an organ being successfully transplanted and an organ becoming unusable [1]. The rest of the paper is organized as follows: In Section 2, we review the literature. Section 3 identifies the current liver allocation system and discusses the proposed model. Section 4 presents the numerical example, comparing the AHP and ANP results and robustness study and finally, the conclusions by proposing some directions for future works are provided in Section 5.

2. Literature Review

2.1 The Analytic Hierarchy Process, Analytic Network Process and the transplant community

There are growing demand for organ transplantation and insufficient supply of organs, and the high cost for transplant procedure which indicates the importance of organ allocation decisions. The Analytic Hierarchy Process (AHP) is a general problem solving technique which is user friendly and easy to both understand and implement and because of this its application in organ transplant was extended. Cook et al. discussed the use of the AHP to develop a rating system allocation of cadaver livers for orthotropic transplantation [6]. In their study five major criteria for comparison were established, defined, and rated relative to one another: logistic considerations, tissue compatibility, waiting time, financial considerations, and medical status. Koch developed an AHP model that includes medical and social criteria in an effort and he concluded that the impact of prescriptive criteria should not be ignored [7]. Koch and Rowell [8] reported a pilot study at the Hospital for Sick Children, Toronto, on a methodology combining qualitative and quantitative data. They used group AHP, to analyze survey-based organ transplant eligibility criteria. In another research they [8, 9] used of qualitative and quantitative criteria again and employed the group AHP and they analyzed the results using Expert Choice software. They concluded that, qualitative and quantitative analysis map barriers to practical consensus in a way not previously possible. Recently, Lin et al. used AHP for the same problem and also they overcame some limitations of a single type of systems, by integrating the views of several organ allocation philosophies [1].

On the basis of the past research, it is clear that the AHP is a valuable tool to tackle the problem at hand but it is not sufficient and precise [3]. While the AHP represents a framework with a uni-directional hierarchical relationship, the ANP allows for complex interrelationships among decision levels and attributes [28]. The upper level node in AHP does not depend on the lower levels and the elements present in a node are also independent of each other. This one sided network fails to capture the complex interactions and feedbacks which might be present in the system [3]. Many decision problems cannot be structured hierarchically because they involve the interaction and dependence between elements. Not only does the importance of the criteria determine the importance of the alternatives as in a hierarchy, but also the importance of the alternatives themselves determines the importance of the criteria. Thus, in ANP the decision alternatives can depend on criteria and each other as well as criteria can depend on alternatives and other criteria [3]. To get rid of this limitation, the present problem is modeled using Saaty’s Analytic Network Programming (ANP) [5]. The ANP is a coupling of two parts: The first consists of a control hierarchy of criteria and sub-criteria that control the interactions. The second is a network of influences among the elements and clusters [5]. ANP has been used in solving many complicated decision-making problems because it is a comprehensive multi-purpose decision making method. There are many studies and applications on ANP but its application in prioritization of organ transplant patients is new. A multitude of papers discuss organ allocation processes and procedures and how to ensure the process is fair and equitable, but none have provided a comprehensive treatment with considering feedbacks and interfaces within and between criteria like the one presented in this paper.

2.2 Organ allocation policies

Different organ allocation policies have been compared in several papers we will discuss more about that in this part. Merion et al. in their study mentioned that, rather than relying solely on the risk of pre-transplant death, the survival benefit among candidates should be considered as a component of allocation policy in order to direct organs to those...
most likely to benefit from the procedure [11]. However Schaubel et al. found that transplantation of high donor risk is effective for high scoring but not for low-scoring MELD candidates [20]. In another study Schaubel et al. found that models that incorporate benefit have better results [12]. Neuberger discussed allocation policies designed to enhance transplant benefit in liver transplantation. He stated that a benefit-based model should have minimum requirements that include being robust and time dependent, and he concluded that organizations are not yet ready to allocate organs according to benefit but the time is not far off when that option can be considered [10]. Lim et al. in their review discussed whether the implementation of utility-based allocation strategies to maximize graft outcomes is an appropriate way forward to provide a better balance between utility and equity in the distribution of deceased donor kidney [13]. Segev in his study highlighted the role of various utility-based options for kidney allocation, including life years from transplant (LYFT), age matching and potential alternative systems and he suggested LYFT as a potential measure [14]. Many studies in the literature (in the organ allocation) are founded on urgency-based models. The urgency-based approach focuses on the Model for End-Stage Liver Disease (MELD) which measures the 3-month survival rate for patients on the waiting list, with highest priority given to patients with the smallest chance of survival [1]. Fink et al. concluded that an allocation process based on MELD rather than clinical judgment would significantly alter organ allocation in Australia and may reduce waiting list mortality [18]. Additionally, Wiesner et al. and Kamath et al. analysed the use of MELD and indicated that MELD score is an extremely powerful predictor of the probability of death in patients with chronic liver diseases [15-17]. Cholongitas and Burroughs explained that other than urgency, the two other types of models utility and benefit have to be considered [19]. They mentioned that well-designed prospective studies and simulation models are necessary to establish the optimal allocation system in liver transplantation, as no current model has all the best characteristics. Cholongitas et al. in their study highlighted that a well matched allocation is better than an urgency-based system and suggested that a clear mismatch should not be considered or allowed [21]. We believe that a comprehensive allocation model using the ANP method can help to overcome the shortcomings and highlight the strengths of each model. The current liver allocation procedure and proposed model are described in detail in the next section and a numerical example illustrates how it can be used.


3.1. Current liver allocation procedure

Since allocation of pediatric patients follows a different algorithm, in this study will not be considered. Then for the adults, liver allocation system assigns points to (adult) patients on the waiting list and gives priority to those with the highest number of points [1]. Livers are first allocated to patients with fulminant liver failure with less than 7 days to live (1A), then patients with the highest MELD scores (1B). For matching some criteria are considered including Size of organ, ABO matchability (blood type compatibility of the donor and recipient), time waiting and mortality risk score. Several matched candidates are notified of their rank in order to consult with their medical support to determine whether to accept or reject an organ [22]. Figure 1 illustrates the process of donor allocation.

![Donor allocation flowchart](image-url)
3.2. Proposed model: Prioritization of Organ Transplant patients using ANP

As we mentioned, because of complex interrelationships between criteria in this study, we model our prioritization problem as an ANP model and in numerical example section we compare proposed ANP model with previous AHP models. The proposed model will consider weights (based on literature) to each criteria and sub-criteria in a network, with the objective of prioritizing and matching patients to donor livers. Figure 2 shows the evaluation network and criteria and sub-criteria. In this paper we use four main criteria and 16 sub-criteria. The four main criteria are medical urgency [24], efficiency [14], transplant benefit [12] and equity [25]. We briefly explain ANP approach in four phases [28, 5, and 3], and detailed explanation of ANP can be found in Saaty [5]:

Phase 1: Construction of model and problem structuring; in this step the problem should be stated clearly and decomposed into a rational system like a network [See figure 2 for this study].

Phase 2: Pairwise comparisons and priority vectors: In ANP, like AHP, pairs of decision elements at each cluster are compared with respect to their importance towards their criteria. In addition, interdependencies among criteria of a cluster must also be examined pairwise. The relative importance values are determined with Saaty’s scale.

Phase 3: Formation of Supermatrix: A supermatrix is a partitioned matrix, where each matrix part represents a relationship between two clusters in a system. The supermatrix concept is similar to the Markov chain process. To obtain global priorities in a system with interdependent influences, the local priority vectors are entered in the appropriate columns of a matrix.

Phase 4: Synthesis of the criteria and patients’ priorities and selection of the best patient: The priority weights of the patients can be found in the normalized supermatrix.

**Figure 2: Proposed ANP model for prioritizing patients for organ allocation.**

3.2.1. Descriptions of criteria and sub-criteria

For better understanding the proposed model the descriptions of criteria and sub criteria is briefly explained in the followings:

**Urgency:** Urgency estimates pre transplant mortality risk which means patients with higher pre-transplant mortality risk on the waiting list are given higher priority for receiving the organ for transplantation [1] and urgency is measured by the predicted number of months of life during the next year without transplant [24]. The urgency policy uses objective lab test results combined with chronic disease information [1]. The three relevant urgency-based metrics that will be considered in this research are the MELD, Child–Turcotte–Pugh (CTP) score and the United Kingdom model for end-stage liver disease (UKELD). (Because of the debates in the literature over the optimal measure for urgency, we incorporate all three metrics into the model).

**Efficiency:** It aims to increase the life prolonging potential of organs and avoids extreme mismatch of donor or recipient [1]. Expected post-transplant outcome by taking into account the donor and recipient characteristics is emphasized in the efficiency-based system [21]. The four relevant efficiency-based metrics that will be considered in
this study are Life years from transplant (LYFT), Matchability, Survivability, and Compliance (Compliance assesses the patient’s ability or willingness to abide by post-transplant treatment directed by medical staff [1]).

**Benefit:** The benefit can be explained by the concept of urgency and utility and accounts for how the patient can experience life after a transplant [1]. Based on Berg et al., allocating an organ to the patient with the greatest transplant survival benefit will minimize mortality as a whole [26]. The four relevant benefit-based metrics that will be considered in this study are: Life year gain (according to OPTN Committee the transplant benefit is defined as the life gained with transplantation as opposed to life without transplantation. In particular, an organ is allocated to the patient who is predicted to have neither the greatest post-transplant lifetime nor the most urgency but the greatest difference between the two [1]), Physical independence (this is a measure of postoperative ability to live a normal and productive life, with higher levels preferred [1]), Intelligence quotient (IQ), and Recognition (Many people believe that prominent and distinguished citizens should be recognized and treated differently [27]).

**Equity:** Fair and neutral allocation of organs to recipients refers to Equity. We considered equity concerns as following sub criteria: Location of residency, Time in waiting, Days since last transplant, Age, and Gender/racial equity. An equitable allocation model should discern such inequalities and maintain a high level of organ acceptability [1]. We acknowledge the existence of these criteria in the model but treat every patient as equal.

3.2.1.1. **Determining weighting values for criteria and sub-criteria**

Once all criteria and sub-criteria have been identified, their relative importance can be determined with respect to their goal or their upper-level criterion using Saaty’s eigenvector technique [29]. The matrix of comparisons is then used to generate sets of weights by using eigenvector scaling in which the columns of the matrix are summed and normalized. The average of each row is calculated to derive the normalized principal eigenvector. Table 1 shows the weighting values for all criteria and sub-criteria in the model. In this paper we obtain the weights for criteria and sub-criteria based on Lin et al.’s [1] study. Participants in the development of their study include a nurse, a bioethicist, a medical resident, a physician and a social worker. The values given here represent experts’ opinion; results may differ with the participation of a different group of experts.

<table>
<thead>
<tr>
<th>Urgency (0.31)</th>
<th>Efficiency (0.28)</th>
<th>Benefit (0.25)</th>
<th>Equity (0.16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MELD (0.741)</td>
<td>CPT (0.123)</td>
<td>UKELD (0.136)</td>
<td>LYFT (0.2)</td>
</tr>
<tr>
<td>Matchability (0.3)</td>
<td>Survivability (0.29)</td>
<td>Compliance (0.21)</td>
<td>Life-gained (0.5)</td>
</tr>
<tr>
<td>Phys. Indep. (0.2)</td>
<td>IQ (0.14)</td>
<td>Recognition (0.16)</td>
<td>Gender &amp; Race (0.01)</td>
</tr>
<tr>
<td>Months in Wait (0.25)</td>
<td>Location (0.4)</td>
<td>Months since last transplant (0.24)</td>
<td>Age (0.1)</td>
</tr>
</tbody>
</table>

4. **Numerical Example**

In this section, a numerical example is used to illustrate the proposed approach. The proposed model in this paper incorporates all suggested criteria [24, 14, 12, 25, 1]. We choose 5 patients with different situations in the organ transplant waiting list to prioritize them using proposed model. The constructed network structure of ANP which is constructed according to the opinions of experts is shown in Figure 3. In this structure the goal is prioritizing patients for organ allocation, four main criteria are Urgency, Efficiency, Benefit and Equity and the five patients are shown as alternatives. The overall priorities of the patients calculated by the ANP are shown in Table 2. The results obtained through Super Decisions software version number 2.0.8. In this example according to the ANP-based analysis, patient 3 has the highest priority for transplant. In the next part we compare the results of AHP and the proposed ANP model.
4.1. Comparing the AHP and ANP results

In this part we compare our model with the hierarchical model for the case under study. Indeed, both AHP and the proposed ANP framework recommend patient 3 as the one in first priority for transplantation. The top ranked patients by AHP are (3, 1, 4, 2 and 5), whereas the proposed ANP model gives the order of (3, 1, 2, 4, and 5). The overall priorities and ratings computed for the all patients are presented below in Table 2 and Table 3. Comparison of results shows that there are significant differences of patients’ prioritization for organ allocation between AHP and ANP outcome derived from interdependencies, outer dependencies and feedbacks. The robustness of our model is verified and described in the next section.

Table 2: Ranking by ANP

<table>
<thead>
<tr>
<th>Graphic</th>
<th>Alternatives</th>
<th>Total</th>
<th>Normal</th>
<th>Ideal</th>
<th>Ranking</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patient 1</td>
<td>0.1393</td>
<td>0.3087</td>
<td>0.9793</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Patient 2</td>
<td>0.0710</td>
<td>0.1574</td>
<td>0.4995</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Patient 3</td>
<td>0.1422</td>
<td>0.3152</td>
<td>1.0000</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Patient 4</td>
<td>0.0660</td>
<td>0.1464</td>
<td>0.4643</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Patient 5</td>
<td>0.0326</td>
<td>0.0723</td>
<td>0.2292</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 3: Ranking by AHP

<table>
<thead>
<tr>
<th>Graphic</th>
<th>Alternatives</th>
<th>Total</th>
<th>Normal</th>
<th>Ideal</th>
<th>Ranking</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patient 1</td>
<td>0.1518</td>
<td>0.3036</td>
<td>0.9383</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Patient 2</td>
<td>0.0668</td>
<td>0.1336</td>
<td>0.4128</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Patient 3</td>
<td>0.1618</td>
<td>0.3236</td>
<td>1.0000</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Patient 4</td>
<td>0.0834</td>
<td>0.1668</td>
<td>0.5155</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Patient 5</td>
<td>0.0362</td>
<td>0.0724</td>
<td>0.2238</td>
<td>5</td>
</tr>
</tbody>
</table>

4.2. Robustness study

The proposed ANP model is deemed robust if it obtains the same result (selection of same candidate for organ transplant) under different operating conditions. We employ the various sensitivity analysis combinations and experiment to test the robustness of the system. The quantitative level of each criterion is varied by ±10% of its original value. Thus, the corresponding factor levels for the experiments are as follows: Urgency = [0.279, 0.310, 0.341], Efficiency = [0.252, 0.280, 0.308], Benefits = [0.225, 0.250, 0.275] and Equity = [0.144, 0.160, 0.176]. Each of the
experimental scenarios corresponds to a unique combination of these factors. From the experiments, we find that the proposed ANP model is robust under all various scenarios, and the decision makers should be confident that patient 3 (in this case study) is the optimal choice, even though the derived criteria weights may be imperfect. Therefore there is low risk of choosing the wrong patient for transplant.

5. Conclusion and Future research
In this study, a methodology for finding out the best candidate for liver transplant has been developed using Analytic Network Process. This work overcomes the shortcomings of previous approaches. The proposed ANP model is a comprehensive framework that incorporates existing literature, medical panel opinions and medical policies. It considers both subjective and objective criteria to prioritize and select patients waiting for donor livers. The proposed ANP model is a robust MCDM technique for synthesizing the factors and sub-factors. This technique handles all kinds of relationships existing between criteria and sub-criteria. So this study provides better result than AHP method. The model aids the decision makers in determining strategic priorities to balance medical urgency, efficiency, transplant benefit and equity and also considers feedbacks and interfaces within and between criteria. With this ANP model, a systematic framework can be employed to empower clinical staff and stakeholders to cooperate towards common strategic goals. Enhancements of this study to the existing models and policies can have significant impacts for both the medical community and the public, and also this model can improve quality of care and patient satisfaction and minimize the number of patients that die while waiting for organ transplant.

Although we believe that the presented model is efficient and effective, there are areas for future enhancements. In order to prioritize organ transplant patients, a pair wise comparison has to be done. Since this pair wise comparison is done by humans (in this case medical staff and academicians), there is always an inherent uncertainty and imprecision associated with the mapping of the decision maker’s judgment into crisp values. Which is the main weakness of the proposed model. Future research should extend the current model and use the fuzzy decision variables in place of single numeric values in order to incorporate these inherent uncertainties. Fuzzy set theory may reduce the vagueness associated with decision makers preferences elicited via pairwise comparisons.

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References