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THE CASE OF CYSTIC FIBROSIS

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Abstract

An organ transplantation rule is constructed with a special reference to the controversial procedure of transplantation of lung sections from living donors to cystic fibrosis patients. The rule indicates the minimum probability of success required for transplantation and how it is related to a wide range of factors associated with the well being and objectives of the directly involved recipient, donor and surgeon. (JEL I19, J17, D91)

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TO TRANSPLANT OR NOT TO TRANSPLANT: THE CASE OF CYSTIC FIBROSIS

An organ transplantation rule is constructed with a special reference to the controversial procedure of transplantation of lung sections from living donors to cystic fibrosis patients. The rule indicates the minimum probability of success required for transplantation and how it is related to a wide range of factors associated with the well being and objectives of the directly involved recipient, donor and surgeon. (JEL I19, J17, D91)

I. Introduction

This paper is concerned with decisions on organs' transplantation from living donors to patients. Notable examples are kidney, bone marrow and lung-section transplantations. While it is relatively easy to reach a decision in favour of transplantation of a kidney, or bone marrow, from a living donor to a chronically ill patient, transplantation of lung sections from living donors to cystic fibrosis patients is a non-orthodox and controversial procedure due to its law probability of success. Surgeons involved in this procedure do not enjoy a wide support in the medical circles. They bear much of the professional and moral responsibility for the operation and its outcome. Their reputation is disputed: while being perceived by some people to be sincere and courageous pioneers, they are held by many others as promoters of illusions and solicitors of futile and harmful debate and altruistic actions within families in grave situations.

The paper's objective is to develop a decision rule on transplanting organs from living donors to patients that can help surgeons, patients, potential donors and medical administrators involved in controversial cases reach a decision in a comprehensive manner. The decision rule developed in the following sections offers a method for assessing the minimum probability of success required for proceeding with the organ transplantation. The proposed method is comprehensive in the sense that it takes into account a wide range of aspects affecting the well being of the individuals most intimately and directly involved: the patient, the donor and the surgeon.

Before proceeding to the construction of the transplantation rule and to the analysis of its properties, a brief medical introduction might be of a value for the readers. Cystic fibrosis is an inherited disease triggered if, and only if, both parents carry the responsible defective gene. The

genetic irregularity leads to a lack of ciliary action in the bronchial tubes of the lungs. Thick mucus collects in the base of the sufferer's lungs, obstructing the smaller air passages and leading to severe respiratory and permanent damage to the lungs, high blood pressure and chronic heart strain. The abnormally thick, viscus mucus also tends to obstruct the pancreas and sweat glands and thus leading to poor digestion and malabsorption of a number of important nutrients and to a loss of large amounts of salt. (See also Smith, 2001.)

Death at early age of cystic fibrosis patients is inevitable. Removal of the patient's lungs and transplanting sections of healthy lungs may improve the quality and lengthen the expectancy of the patient's life. Presently, the rate of success is low. Since the cystic fibrosis patient's physical fitness deteriorates over time, a delay of operation is resulted in even lower probability of success.

In view of the short supply of suitable lungs from deceased people and the diminishing probability of success associated with delay, living donors are required. Parents cannot be considered as preferred donors as they are carriers of the defective gene causing the disease and, in some cases, also due to their advanced age. In most of the cases involving adult cystic fibrosis patients, the donors are siblings who are not carriers of the trait. This close kin relationship explains the willingness of the donors to participate in a low-success-rate procedure. It also reduces the likelihood of rejection of the transplanted lung sections.

Transplantation of lung sections obtained from living donors is an experimental procedure. It is voluntarily applied in some cases of young adult and adolescent cystic-fibrosis patients. It involved the removal of the damaged lungs of the patient and the implantation of the lower sections of the right and left lungs and, in some cases, also a small heart tissue. Presently, the probability of significant improvement in the recipient's health and life expectancy is low, and recipients die from infections, haemorrhages and other complications. In addition, the donors experience a significant loss of potential physical fitness and health due to the reduction in their lungs' capacity and due to the pain, traumatic effect and the complications accompanying the incision. From the medical industry's perspective, knowledge is gained through learning by doing, and improved knowledge may raise the probability of success in future operations. This

inter-temporal positive externality provides a further incentive to transplant despite the currently low odds of success and the loss of health for the donors.

The construction of the transplantation rule and the discussion of its properties are structured as follows. The individuals intimately and directly involved in the procedure and their well being are described in section II. The decision rule and the minimum probability of success required for transplantation are presented in section III. The effects of the pre-operation health conditions of the recipient and the donor and the effect of the expected medical knowledge gains on the minimum probability of success required for transplantation are summarised in section IV. The special case where the expected deterioration in the Donor's health is negligible and learning by experimenting on human patients is not an admissible objective for ethical reasons is analysed in section V. The paper is concluded with a brief summary in section VI.

II. The individuals directly involved, their concerns and their well being

The proposed model involved the three essential and cooperatively involved individuals -- the Recipient (R), the Donor (D) and the Surgeon (S). There are, of course, other stack holders -- family members, friends, medical colleagues and administrators and the public. Yet in view of the major uncertain outcomes of the transplantation for these most intimately and directly involved individuals, concentrating on the inner circle is essential. It also simplifies the construction of the transplantation rule and its application. The outcomes of the double operation are uncertain. Yet a much higher level of uncertainty is associated with the outcome of the Recipient's operation than with the outcome of the Donor's operation. It is assumed, for tractability, that the uncertainty associated with the consequences of the Donor's operation to her health are negligible.

II.1 The Surgeon

The Surgeon is taken to be sincere in the sense that she is concerned with the well-being of the Recipient (u^R), with the well being of the Donor (u^D), and with learning (L), *per se*. The Surgeon's overall concern (u^S) is assumed to be a weighted sum of these three aspects:

$$u^S = u^R + g_1 u^D + g_2 L \qquad (1)$$

where g_1 is a positive scalar denoting the Surgeon's degree of concern for the Donor's well being vis-a-vis her degree of concern for the well being of the Recipient (taken as a numeraire) and reflecting no favouritism when $g_1 = 1$; and where g_2 is a positive scalar indicating the Surgeon's degree of interest in learning by doing. For practicality, the possible values of the variables (u^R, u^D and L) in this weighted sum are taken to have an identical range -- a scale of 0 to 10 for instance. Thus, $g_2 > 1$ (alternatively $g_2 < 1$) represents a scenario in which the Surgeon is more (less) interested in learning by doing than the well being of the Recipient. This may not necessarily reflect opportunism and lack of consideration for a patient. It may be explained by a far-sighted approach and strong concern for future patients.

II.2 The Recipient

The Recipient is considered to be generating well being (u^R) from her own health (H^R) and the Donor's health (H^D). Her operation can be either successful or a failure. Thus, the distribution of her well being after the transplantation (u^R_{post}) is given by the following binomial distribution:

$$u^R_{post} = \begin{cases} (1+g_R)H_0^R + b_R(1-d_D)H_0^D & p \\ (1-d_R)H_0^R + b_R(1-d_D)H_0^D & 1\text{-p} \end{cases} \qquad (2)$$

where,

p = the probability of successful operation, $0 < p < 1$,

$1-p$ = the probability of failure,

H_0^R = the Recipient's health before the transplantation,

H_0^D = the Donor's health before the transplantation,

g_R = the rate of improvement in the Recipient's health following a successful operation,

d_R = the rate of deterioration in the Recipient's health in the case of failure,

d_D = the rate of deterioration in the Donor's health due to the operation, and

b_R = the Recipient's degree of concern for the Donor's health, $b_R \geq 0$, with $b_R = 0$ indicating strict selfishness and, in contrast, $b_R > 1$ reflecting an extreme level of concern for the Donor's health.

Thus, the Recipient's expected post-operation well being is

$$E(u^R_{post}) = H_0^R + (g_R + d_R)H_0^R p - d_R H_0^R + b_R(1-d_D)H_0^D. \qquad (3)$$

In other words, the expected improvement in the Recipient's utility from the transplantation ($E\Delta u^R$) is

$$E\Delta u^R = E(u^R_{post}) - \underbrace{(H_0^R + b_R H_0^D)}_{u_0^R} = (g_R + d_R)H_0^R p - d_R H_0^R - b_R d_D H_0^D \qquad (4)$$

where u_0^R denotes the Recipient's pre-operation level of well being – a combination of her own and her Donor's pre-operation health.

II.3 The Donor

The Donor, caring (of course) about the Recipient's health to a degree b_D (vis-a-vis her own health so that $b_D > 1$ reflects an extreme degree of altruism), also faces a binomial distribution of her post-operation well being:

$$u_{post}^{D} = \begin{cases} (1+d_D)H_0^D + b_D(1-g_R)H_0^R & p \\ (1-d_D)H_0^D + b_D(1-d_R)H_0^R & 1\text{-p.} \end{cases} \quad (5)$$

Consequently, the expected change in the Donor's well being induced by the transplantation is

$$E(u_{post}^{D}) - \underbrace{(H_0^D + b_D H_0^R)}_{u_0^D} = b_D(g_R + d_R)H_0^R p - d_D H_0^D - b_D d_R H_0^R . \quad (6)$$

where u_0^D denotes the Donor's pre-operation level of well being – a combination of her own and the Recipient's pre-operation health.

III. The transplantation rule

While the assumption of risk aversion is commonly made in normative behaviouristic models, risk neutrality can be viewed as an objective and, hence, a suitable consideration of uncertainty in the present context of constructing a decision rule which is free of subjective attitude toward risk and hence conservatism. A risk-neutral Surgeon, who is also rational, favours transplantation and seeks the consent of the potential Donor and Recipient if

$$E(u_{post}^{S}) - u_0^S > 0 . \quad (7)$$

In view of this condition and in recalling equations (1), (4) and (6), a decision in favour of transplantation is reached if

$$[(g_R + d_R)H_0^R p - d_R H_0^R - b_R d_D H_0^D]$$

$$+ g_1[b_D(g_R + d_R)H_0^R p - d_D H_0^D - b_D d_R H_0^R] + g_2 L > 0 \quad (8)$$

or, equivalently, if

$$p > \frac{(b_R + g_1)d_D H_0^D + (1+g_1 b_D)d_R H_0^R - g_2 L}{(1+g_1 b_D)(g_R + d_R)H_0^R}. \qquad (9)$$

The term on the right-hand-side of inequality (9) is the critical level of p: if the probability of success is assessed to be higher (lower) than this critical level, a decision in favour of (against) transplantation is reached. This critical level is, therefore, referred to as the minimum probability of success ($p_{\min}$) required for transplantation.

IV. The properties of the minimum probability of success

In order to facilitate the analysis of properties $p_{\min}$ the right-hand-side of inequality (9) is rearranged and equivalently rendered as linearly increasing in the Donor-Recipient pre-operation health ratio and the learning-Recipient's pre-operation health ratio:

$$p_{\min} = \frac{d_R}{(g_R + d_R)} + \left(\frac{(b_R + g_1)d_D}{(1+g_1 b_D)(g_R + d_R)}\right)\frac{H_0^D}{H_0^R} - \left(\frac{g_2}{(1+g_1 b_D)(g_R + d_R)}\right)\frac{L}{H_0^R}. \qquad (10)$$

IV.1 The effect of the pre-operation health

The second term on the right-hand-side of equation (10) indicates that the minimum probability of success required for transplantation rises with the ratio of the Donor's and Recipient's pre-operation health conditions. The term in the parentheses reveals that this (mathematically) positive effect of the Donor-Recipient pre-operation health ratio on the minimum probability required for transplantation is amplified by:

1. the Recipient's degree of concern for the Donor's health (b_R),
2. the expected rate of deterioration in the Donor's health due to the operation (d_D), and

3. the Surgeon's degree of concern for the Donor's well being (g_1) if $b_D b_R < 1$, i.e. if the concerns of both the Donor and Recipient for their own, self health are greater than their concerns for each other health, or, more generally put, if at least one of them is selfish or very moderately altruist towards the other.

However, the positive effect of the Donor-Recipient pre-operation health ratio on the minimum probability required for transplantation is moderated by:

1. the expected rate of improvement in the Recipient's health in the case of success (g_R),
2. the rate of deterioration in the Recipient's health in the case of failure (d_R),
3. the Donor's degree of concern for the Recipient's health (b_D), and
4. the Surgeon's degree of concern for the Donor's well being (g_1) if $b_D b_R > 1$, i.e., if the concerns of both the Donor and Recipient for their own, self health are smaller than their concerns for each other health (extreme degrees of altruism), or, more generally put, if at least one of them is extremely altruist while the other is not completely selfish.

IV.2 The effect of the expected medical knowledge gains

The third term on the right-hand-side of equation (10) suggests that the minimum probability of success required for transplantation is lowered by the ratio of the expected knowledge gains stemming from the operation to the Recipient's pre-operation health. A careful inspection of the term in the parentheses reveals that the moderating effect of the ratio of the expected knowledge gains to the Recipient's pre-operation health on the minimum probability required for transplantation is increased by the Surgeon's degree of interest in learning-by-doing (g_2), but lowered by:

1. the rate of improvement in the Recipient's health in the case of success (g_R),
2. the rate of deterioration in the Recipient's health in the case of failure (d_R),
3. the Donor's degree of concern for the Recipient's health(b_D), and

4. the Surgeon's degree of concern for the Donor's well being (g_1).

V. When the Donor's health is unaffected and experimenting with human patients is inadmissible

In the special case where the expected deterioration in the Donor's health is negligible (i.e.,$d_D = 0$), and where for ethical reasons learning by experimenting on human patients is not thought as an admissible objective (i.e., $g_2 = 0$), equation (10) is reduced to:

$$p_{\min} = \frac{d_R}{(g_R + d_R)}. \qquad (11)$$

In this case, the minimum probability of success required for transplantation is also independent of the Recipient's pre-operation health. It exclusively depends on the expected rate of change in the Recipient's health. The minimum probability of success required for transplantation declines with the expected rate of improvement (g_R) in the Recipient's health following a successful operation, and increases with the expected rate of deterioration (d_R) in the Recipient's health following an unsuccessful operation.

VI. Conclusion

A decision rule on organ transplantation from living donors to patients was developed in this paper. It was developed by taking into account a wide range of factors affecting the well being of the three most intimately and directly involved individuals: the recipient, the donor and the surgeon. The well beings of the recipient and the donor were assumed to increase with their own health, and were also allowed, as should be expected in the case of the donor at least, to rise with the health of each other. The Surgeon was taken to be sincere in the sense of being solely concerned with the well being of the recipient and the donor and, possibly, interested in gaining knowledge through learning by doing. The cooperative integration of the concerns of a rational, risk-neutral (non-conservative) surgeon with the expected changes in the well beings of

the recipient and donor, led to a transplantation decision rule that indicated the minimum probability of success required for transplantation. The minimum probability formula included the pre-operation health conditions of the recipient and donor, the potential knowledge gains, and parameters indicating the expected rates of change in the recipient's and donor's health, the degrees of altruistic attitude of the donor and recipient towards one another, and the relative weights given by the surgeon to the well beings of the recipient and donor and to learning by doing. The application of the proposed organ-transplantation decision rule requires a delicate, careful numerical assessment of these factors and parameters.

Reference

Smith, M.W., 2001. Cystic Fibrosis, http://webmd.lycos.com/content/article/1680.53769.