STRATEGIES FOR EVALUATION OF SUITABLE DONORS: ITALIAN EXPERIENCE

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ABSTRACT
Italy was lacking standardised procedures for donor safety evaluation. We developed practice guidelines, while a panel of experts coordinated by the National Transplant Centre, is available 24 hours a day to support decisions in difficult cases. The guidelines identify five levels of risk and give recommendations for the utilization of donors with HBV and HCV infections as well as for malignancies with negligible or very low risk of transmission. In conclusion we aim to standardize the process of donor evaluation across Italy, to increase the pool of utilised donors and to reduce the risk of communicable disease transmission.

INTRODUCTION
Organ shortage represents one of the major limitation to transplant activity in Italy. The potential for increasing the number of effective donors largely relies on the utilization of new categories of donors. It has been accepted that donation is possible from elderly people and from people with transmissable diseases, provided that some specific conditions are met. However there is not consensus between different transplant centres regarding the criteria for considering an organ suitable for transplantation [1-3].

The main objective of the current initiative was to develop a consensus document for evaluation of organ suitability in Italy. In more detail we aimed to implement practice guidelines for utilization of organs at risk of transmitting infectious or neoplastic diseases taking into account clinical and ethical problems, to monitor the incidence of infectious and neoplastic diseases identified during the donor evaluation process and definitely to increase the utilization rate of potential donors.

METHODS
Incidence of infectious and neoplastic diseases identified during the donor evaluation process were retrospectively measured for the last two years. Results were discussed by a panel of Italian
experts in the field of infectious diseases epidemiology, hystopathology and transplant surgery. The panel met regularly during the current year and developed a consensus document describing risk levels and strategies for early detection of donors who are liable to transmit diseases. The final document was discussed and reviewed with regional coordinators. National Transplant Centre also set up a group of three clinical experts (coroner, histopathologist and infectious disease consultant) available 24 hours a day, to whom transplant centres address for a second opinion in doubtful cases. Records of donors and recipients data are kept in an electronic database which is regularly updated with follow-up data. Analyses will be carried out regularly and results reported to each regional coordinator for further dissemination.

RESULTS

Each Italian region identified the coordinating structure (regional or interregional reference centre) to which all intensive care units as well as local coordinators refer during the reporting procedures of the potential donor. Intensive care operators as well as local coordinators must notify to the regional or interregional reference centre all individuals undergoing the brain death diagnosis process, being ventilated in intensive care units.

The suitability of the potential donor, who will undergo the process of organ removal, must be evaluated by the intensive care operators as well as by local coordinators jointly to the regional or interregional reference centre according with the procedures presented in these guidelines.

Retrospective analysis was conducted on 2682 donors. A total of 78 (2.9%) donors with malignancy were identified in the period 2001-2002.
Of the 78 donors: 37 (47.4%) were detected and excluded before surgical removal, 20 (25.6%) were detected and excluded after organ removal but prior to transplantation, 21 (26.9%) were detected after organ transplantation [4].

The guidelines identified five levels of risk: 1) **Unacceptable risk**: HIV 1-2 infection, HBsAg positivity in presence of documented Hepatitis D virus infection, malignancies (with some exceptions), systemic infections for which there is not effective treatment, documented prion diseases. **Increased but acceptable risk**: cases where transmissible organisms or diseases are identified during the evaluation process, but organ utilization is justified by the recipient specific health situation or by the severity of his clinical conditions. **Calculated risk**: cases where, even in presence of transmissible diseases, transplantation is allowed for recipient with the same disease or with a protective serologic status. **Not assessable risk**: cases where the evaluation process does not allow an appropriate risk assessment for transmissible diseases. **Standard risk**: cases where the evaluation process did not identify any transmissible disease.

Experts from the Italian National Transplant Centre can be consulted if any doubt arises (second opinion). Specific recommendations are given for the utilization of donors with HBV and HCV infections as well as for malignancies with negligible or very low risk of transmission.

HBV positive donors (HBsAg positivity) can be utilised for: a) HBsAg positive recipients, provided that the donor is negative for HDV infection; b) HBsAg negative recipients (with or without protective anti-HBsAg antibody titre), for life-saving organs or in life threatening situations. Donors positive only for HBcAb may not represent a significant risk for organ donations other than liver and their utilization is allowed, after having provided an informed consent, even for patients without protective anti-HBsAb. On the other hand, the livers of these donors have an high risk of HBV transmission to the recipient (approximately 50%). Therefore it
is necessary to monitor the recipient over time, to administer prophylactic treatment with lamivudine and to provide an informed consent.

In case of donors with HCV infection we recommend to use their organs for recipients with the same infection, while for HCV negative patients, these organs should be used only in emergency situations and after having signed an informed consent.

Renal transplantation from an HCV positive donor to an HCV negative recipient is never justified.

With regard to malignancies transmission, we considered as cancers with negligible risk those for which transmission has been never demonstrated (i.e. carcinoma in situ, basal cell carcinoma, cutaneous squamous cell carcinoma without metastases, carcinoma in situ of the cervix, carcinoma in situ of vocal cords, urothelial papillary carcinoma (T0 according to the TNM classification)). On the other hand, cancers with very low risk are those for which transmission cannot be completely excluded but the risk is much lower than the potential benefit deriving from transplantation (i.e. prostate asymptomatic adenocarcinoma, follicular thyroid carcinoma of low invasiveness, papillary thyroid carcinoma). In theses cases transplant centres can decide to utilise organs, upon patient informed consent, provided that a closed follow-up and clinical monitoring is ensured.

**CONCLUSIONS**

Standardization of donor evaluation process is a priority for National Transplant organizations. Italian National Transplant Centre has implemented a document to uniform the management of donors in Italy taking into account the increasing number of “marginal” donors. The follow-up analysis of recipients will allow to measure the level of risk related to different procedures and to estimate the validity and effectiveness of this guidelines. In conclusion organs from donors with
cancer or infectious diseases should not be routinely discharged, recipient medical urgency or specific clinical conditions must be always taken into account as well as his/her willingness to receive a marginal organ.

REFERENCES


