Impact of donor age on the outcome of intestinal transplantation in Japan

Abstract

The donor age for intestinal transplant (ITx) is relatively younger than that for other solid organs. Clear criteria for adequate donors has not been established. Only few donor has been available due to shortage of young donor. In order to clarify the age of the cadaveric and living donor, we reviewed the outcome of ITx based on donor ages in Japan. Standardized report forms were sent to all known ITx programs, asking for information on intestine transplants performed between 1996 and 2016. All programs responded. Patient and graft survival estimates were obtained using the Kaplan-Meier method. Five institutions provided data on 27 grafts in 24 patients. There were 14 cadaveric and 13 living donor transplants. The median age of donors for ITx was 40 year old (17 to 60 years). The graft survivals at 5 years were 66% over 40 year old (n=18) whereas 47% under 40 year olds (n=9). There were no stastically difference. (p=0.49). Graft survivals at 5 years were 60% over 50 year old (n=5) whereas 57% under 50 year olds (n=22). There was no significant difference (p = 0.27). There is no difference in survival between the donor age under and over 40 years old. The donor age of ITx can be expanded to over 40 years old up to 50 years old. It may help to improve donor shortage. In the future, it is necessary to clarify the donor criteria for ITx by accumulating data on ITx.

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Introduction

The prognosis of intestinal failure (IF) has improved dramatically owing to the development of parenteral nutrition (PN). However PN-related complications, such as central venous catheter infection, venous access thrombosis, and IF associated with liver disorder are still major causes of mortality in patients with IF. However, patients who develop life-threatening complications are considered for intestinal transplantation (ITx). ITx, which can significantly improve their prognosis and quality of life, has become an established treatment for IF[1]. More than 2800 ITx have been performed worldwide [2].

Clear criteria for adequate donors has not been established. We have defined that donor age criteria was under 40 years old for ITx because more than 90% of the donor age of ITx in the US were under 34 year old,[3] however only few donor has been available due to shortage of young donor in Japan. In order to clarify the age of the cadaveric and living donor. We reviewed the outcome of ITx based on donor ages in Japan

Methods

ITx have been performed in Japan since 1996. We performed prospective cohort multi institutional study using web based questionnaire. All intestinal transplantation

programs registered all intestinal transplants performed between 1996 and December 31, 2016 in Japan. Donor age, recipient age, graft type and outcome were gathered.

Data were analyzed using the JMP Ver.11 software package (SAS, USA). Patient and graft survival estimates were obtained using the Kaplan–Meier method. For survival analysis, failure was defined as occurring on the date of graft removal or death. Wilcoxon test were used for Kaplan Mayer survival curve analysis. A P value less than 0.05 was considered statistically significant. This study was approved by the Osaka University Hospital institutional review board and was supported by Japan Agency for Medical Research and Development.

Results

Five institutions provided data on 27 grafts in 24 patients. There were 14 cadaveric and 13 living related donor transplants. The median age of donors for intestinal transplant was 40 year old (17 to 60 years). Over all patient survival was 88% at 1 year, 70% at 5 year and 62% at 10 years after intestinal transplantation. Over all graft survival was 81% at 1 year, 57% at 5 year and 40% at 10 years after intestinal transplantation. The outcome of intestinal transplant has been improved but it was poorer than that of other organ transplant.

Graft survivals were assessed by donor age. Over all graft survival were compared

in each age group. Age groups were divided by 40 and 50 year old. Patient demographic / clinical futures in each age groups were shown in Table.1. A Kaplan Mayer survival curve that the donor age group were divided by 40 year old was shown in Fig.1. Graft survivals at 5 years were 66% over 40 year old whereas 47% under 40 year olds. There were no stastically difference. (p=0.49). Graft survivals at 5 years were 61% over 30 year old whereas 52% under 30 year olds. Graft survivals at 5 years were 60% over 50 year old whereas 57% under 50 year olds. There were no stastilally deference in divided at 50 year old (p=0.26) as well. There was no stastically change in over all graft survival by donor age.

In the cadaveric donor, the median age was 38 years old (17 to 58 years), Cadaveric graft survival were compared in each age group. Age groups were divided by 30 and 40 year old. The graft survival rate at 5 years after transplant by donor age was 67% (n=7) under 40 year old and 57% (n = 7) over 40 years old in cadaveric donor. Fig.2 There was not significantly different (p = 0.65). There was no significant difference (p = 0.84). There was no survival of donors over 50 years old. Younger donors showed better survival but no statistically significance.

In the living donor it was 42 years old (21 to 60 years). Living graft survival were compared in each age group. Age groups were divided by 40 and 50 year old. The graft survival rate at 5 years after transplant by donor age was 20% (n=5) under 40 year old and

50% (n = 8) over 40 years old in living donor. There was significantly different (p = 0.045) in Fig.3. The graft survival at 5 years was 48% (n=10) under 40 year old and 66% (n = 3) over 40 years old in living donor. There was no significant difference (p = 0.93). Older donors showed better survival but no statistically significance.

The recipient age under 40 year old donor was mean 13.3 year old (ranged 0 to 35 year old) whereas that over 40 year old was mean 17.5 year old (ranged 6 to 29 year old). There was no stastically significant (p= 0.31). In cadaveric donor ITx, the recipient age under 40 year old donor was mean 21.4 year old (ranged 10 to 35 year old) whereas that over 40 year old was mean 18.6 year old (ranged 6 to 29 year old). There was no stastically significant (p= 0.56). In living donor ITx, the recipient age under 40 year old donor was mean 2 year old (ranged 0 to 4 year old) whereas that over 40 year old was mean 14.5 year old (ranged 10 to 27 year old). The recipient age under 40 year old donor was younger stastically significant (p= 0.0002).

Discussion

Since the intestine is very sensitive to ischemia, hemodynamically stable donors have been traditionally preferred. The donor age for ITx is relatively younger than that for other solid organs. Although there are relatively few candidates for ITx, the waiting time is

relatively long. Among candidates listed in 2012-2013, median time to transplant was 11.3 months for adult and 7.3 months for pediatric intestine-liver transplant candidates, and 3.6 months for adult intestine transplant candidates. The median for pediatric ITx candidates listed in 2008-2009 was 19.7 months in US data[3]. In the past, intestinal transplant teams could be selective in choosing donor organs for 2 reasons; first, the supply of potential intestinal grafts far exceeded the comparatively low demand and second, there were few if any criteria for defining the "marginal" intestinal graft. However, as ITx has become increasingly common, the "luxury of selectiveness" in graft procurement has diminished greatly, thereby requiring consideration of extended donor criteria in ITx, similar to the evolution of transplantation of other solid organs.

The ideal donor for ITx is younger than 50 years [4-7]. Donors older than 50 years are considered extended criteria donors. Some programs reported marginal donor organs have been used successfully.[4, 6] Based on US ITx donor data, more than 90% of donor age was under 34 year old.[3] We applied more strict criteria because of little experience of ITx. Donor age less than 40 year old seemed to be suitable donor previously in Japan. The Japanese experience has been similar. The mean donor age was 37 years old, with 2 donors over the age of 50[8]. Among living donors, the maximum age allowed was 60 years [9].

Young graft showed better graft survival in cadaveric donor. But no statistically

significance. Furthermore older donor showed better graft survival in living donor. It may result from elder recipient in old donor. ITx in very young child resulted in poor outcome. Candidates for ITx are usually small body size due to failure to thrive. Especially intra-abdominal space is small in short gut syndrome. Therefore small donor including pediatric donor in some case are recommended.

In our experience there were no change in graft survival by donor age. Marginal donor organs in terms of donor age should not be discarded.

Conclusions

There is no difference in survival between the donor age under and over 40 years old. The donor age of ITx can be expanded to over 40 years old up to 50 years old. It may help to improve donor shortage. In the future, it is necessary to clarify the donor criteria for ITx by accumulating data on ITx.

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