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GENDER DIFFERENCES IN SURVIVAL DURATION FOLLOWING LIVER TRANSPLANTATION

Psychiatry

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ABSTRACT

Possible disparities between men and women with respect to post liver transplant survival were investigated in a twenty-two year study with 489 male and 258 female patients. The guiding hypothesis was that estrogen levels in women facilitate prolonged survival durations compared to those of men but that this protection may wane with age and reduced estrogen resulting from menopause. Kaplan-Meier survival analysis supported longer survival rates by females. Median duration values were 123 and 160 months respectively. Furthermore, Cox regression procedures corroborated these findings with the control of age at the time of transplantation. The related hazard ratio indicated that male gender was associated with a 64% increase in the probability of post-transplant death.

KEYWORDS

transplantation, survival, gender

Introduction

The human liver is an organ with receptors that respond to sex hormones (Pillay, et al., 1990). There is evidence in this regard that estrogen can be a protective factor that facilitates more prolonged survival durations among female transplant recipients. Indeed, survival duration studies (e.g., Duffy, et al., 2010; Jain, et al., 2000) have reported that women generally live longer after liver transplantation then men. Such findings are congruent with the notion that estrogen provides protection against post-transplant medical complications such as osteoporosis and fibrosis (Rodriquiz-Castro & De Martinet, 2014).

Investigations that have not found gender differences in survival can also be interpreted in terms of the "estrogen protection" hypothesis. For example, Pillay, et al., (1990) found no survival differences by gender in child transplant patients prior to the onset of puberty. A commensurable hypothesis is that post-menopause status of older female transplant patients will lead to diminishing degrees of estrogen protection together with weight gain propensities that may be hazardous to post-transplant survival (Rodriquiz-Castro & De Martin, 2014). Thus age at the time of transplant may be a factor in determining whether gender differences in length of survival obtain.

Method

The participants were 747 patients who were the recipients of liver transplantation across a 22-year time period (1993-2015). There were 489 men (Mean age = 52.68; range = 18-75) and 258 women (Mean age = 50.61; Range = 20-75). Recorded data included age at the time of transplantation and the time period between transplantation and death.

Two approaches to data analysis were employed. The Kaplan-Meier survival model was used to directly compare survival rates of males and females with reference to survival curves. Significance tests were "Tyrone-Ware" involving a statistical comparison during the middle range of the survival curves and the "Log Rank," that evaluated differences in the later ranges (Clark, Bradburn & Alton, 2003). The Cox proportional hazards survival model in contrast provides data regarding the hazard or risk of dying during the post-transplant time period. Moreover, the Cox procedure allows statistical control of variables of concern. In the current study, the hypothesis of interest was whether or not gender differences are found when age at transplant is held constant.

The Cox approach yields a hazard ratio that is similar to the "odds ration" in logistic regression. A significant hazard ration beyond 1 indicates an increasing probability of death for the variable being investigated (Connell, 2012).

Results

A statistically reliable male-female difference was found via the Kaplan-Meier procedure both in the middle and later survival stages (Tyrone-Ware = 21.88, df = 1, p <.0001; Log Rank = 20.80, df = 1, p <.0001). The median data presented in table 1 exemplify the magnitude of gender differences in duration, with women surviving almost three years longer then men.

Table 1 Median Survival Times

Gender	Median Survival Estimates In Months	Standard Error	95% CI	
			Lower	Upper
Male	123	5.59	112.03	133.97
Female	160	16.12	128.39	191.60
Overall	140	7.34	125.62	154.38

The question remained regarding whether the survival advantage for women would be maintained with the age at transplantation controlled. Again, reductions in estrogen levels with age may be hazardous to women such that the advantage may dissipate.

Table 2 Hazard Ratios for Age and Gender

Variable	B	SE	Wald	df	p	Exp(B)
Age	.015	.006	6.04	1	.014	1.015
Gender (male)	.594	.138	18.44	1	<.0001	1.812

The Significant hazard ratios presented in table 2 indicate that age at the time of transplant increases the probability of dying. Perhaps more importantly, after controlling for the age variable, being male increases the chances of post-transplant death by approximately 64%. The graphic hazard display in figure 1 with the upper curve indicating a higher probability of death for men, further illustrates this finding.

Discussion

Women simply do better then men in post-transplant survival. The current study adds credence to such a finding. It may be that the estrogen-protection hypothesis is the ascendant explanation for this phenomenon. An interpretation consistent with this notion is that males may have adverse consequences when there is a gender "mismatch" between donor and recipient. That is, when a male receives a female liver, there may be a disruption of the gender-specific hormonal milieu that will affect the individual's survival functions (Pillay, et al., 2010). A credible alternative however is that females for a variety of reasons, donate livers that are lower in quality (e.g., women are typically older than male donors; Burra, et al., 2013). A limitation of the current investigation is the unavailability of information on donor organs.

Liver quality, hormonal disparities, causes of death, and life style

discrepancies are among the variables that require investigation to foster better understanding of gender differences in post-transplant survival.

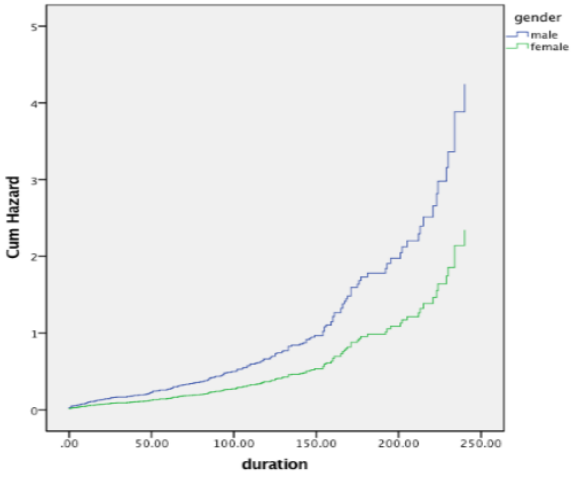

Fig. 1. Comparison of Hazard Curves for Men and Women Controlling for Age at Time of Transplant

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