

# Post-traumatic growth in survivors of allogeneic hematopoietic stem cell transplantation

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## Abstract

**Objective:** This study aimed to understand factors related to post-traumatic growth (PTG) in patients who received allogeneic hematopoietic stem cell transplantation (HSCT), building baseline data for developing intervention programs to enhance PTG in HSCT survivors.

**Methods:** A self-report survey was administered to 100 patients who received HSCT within the last 5 years. The Post-traumatic Growth Inventory, Impact of Event Scale—Revised, Perceived Social Support Scale, and Healthcare Professional's Support Scale were used, as well as items on demographic and clinical characteristics. Standard deviations of frequency and percentage, Chi-squared test between genders, independent *t*-test, correlation analysis between independent variables and extent of PTG, and regression analysis were conducted.

**Results:** The PTG levels of HSCT survivors were statistically significantly higher when participants were women, carried out more religious activities, had higher educational levels, or utilized nurse counseling. The 'intrusive thinking' traumatic impact subcategory, as well as social support and support from healthcare professionals, were found to be highly related to PTG scores. Upon multiple regression analysis, factors with greatest influence on PTG in HSCT survivors were support from healthcare professionals, followed in order, by social support, utilization of nurse counseling, intrusive thinking, and frequency of religious activities.

**Conclusions:** We suggest implementing programs for HSCT patients to enhance support from healthcare professionals and to increase post-traumatic growth through greater utilization of nurse counseling, self-help meetings, and writing.

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Received: 19 April 2014

Revised: 12 October 2014

Accepted: 15 October 2014

## Background

Allogeneic hematopoietic stem cell transplantation (HSCT) is one of the treatments for hematologic diseases such as leukemia, lymphoma, and myelodysplastic syndrome. Annually, approximately 40,000 cases of HSCT are conducted worldwide, with roughly 2,000 in South Korea. The number of HSCT survivors is increasing by tens of thousands each year [1,2].

Hematopoietic stem cell transplantation is an extremely stressful event and patients experience not only adverse effects from pre-conditioning medications prior to transplantation but also graft-versus-host disease (GVHD), anxiety, depression, sexual dysfunction, problems returning to work, and difficulties building social relations [3,4]. These are experienced for a considerable amount of time after the transplantation and can lead to decreased quality of life [3]. Prior studies have reported development into post-traumatic stress disorder in 5–19% of survivors with the characteristics of avoidance, hyper-arousal, emotional numbing, and re-experiencing the event [4].

However, there is a growing interest in the possibility of positive changes in life values, expansion of interpersonal relationships, increased sense of intimacy, and self-image

in response to severe stress events. Various terms, such as benefit finding, perceived benefits, stress-related growth, resilience, and positive psychological changes have been used to describe the positive psychological changes in people who overcome trauma and show recovery over time from the traumatic event. Tedeschi and Calhoun referred to this as 'post-traumatic growth' (PTG) [5]. PTG acts as a buffer to maintain psychological stability after traumatic experience, which may include not only accidents, war, and natural disasters but also cancer diagnosis and treatment [6]. This process has been proposed to occur through deliberative rumination and indicate growth beyond pre-trauma levels [7–9]. Event rumination does not stop at simply recalling the event; it has been proposed to develop into higher order thinking that examines the meaning of the event and its impact on life. Consolidating one's life before and after the event and reconstructing one's beliefs occur and can lead to PTG [7].

Previous studies have reported that cancer diagnosis and treatment are perceived as a traumatic events and that cancer patients and survivors also experience PTG [6]. However, the majority of these studies examined breast cancer survivors, who show a higher level of PTG than survivors of other cancer types [10–13]. Such findings

suggest that PTG level varies depending on cancer type, cure rate, and form of treatment. PTG levels were shown to be lower in patients suffering from cancers with poor prognosis, such as lung or cholangiopancreatic cancer, as well as cancers with low quality of life, such as head and neck cancer [14,15].

In contrast, the few studies that have focused on PTG in HSCT survivors have combined both allogeneic and autologous HSCT survivors [16,17], despite the two types possessing different post-transplantation complications and self-management strategies. Hence, it is difficult to determine the extent of PTG after traumatic events in allogeneic HSCT survivors alone. Although another longitudinal study demonstrated that PTG level increased with the length of time since HSCT [18], there were limitations with a high drop-out rate and lack of other longitudinal studies, making comparison impossible.

There are conflicting results on the relationships among cancer severity, time elapsed since the traumatic event, and PTG. Some studies have shown traumatic events with greater severity to lead to higher PTG levels [11,16], whereas others have reported no relationship [12]. Although the number of longitudinal studies is limited, there are reports indicating that higher levels of PTG come with longer elapsed time [18,19]; still, other reports indicate otherwise [14,17].

Different studies have reported different results for relations between socio-demographic characteristics and PTG levels. Reports on correlations between gender or religious activities and PTG are relatively consistent, with women showing higher PTG levels than men in many previous studies. The reason for this has been determined to result from women are more likely to engage in event rumination—a precursor to PTG—more frequently than men, receive emotional relief and support from others by revealing themselves more, and attempt more frequently to find the event's meaning in their lives [9,12,18,20]. Age, however, is the most controversial; previous studies reporting higher PTG levels in younger survivors suggested that experiencing diagnosis and treatment of a life-threatening disease at such an early age leads to integrative thinking about the purpose of life, leading to higher PTG levels [10,16,21]. On the other hand, a study reporting high PTG levels in older individuals following HSCT suggested that older individuals are more likely to have greater appreciation than younger people for their peaceful lives prior to transplantation, and would have maintained a wider network of interpersonal relationships from longer life experiences, leading to higher PTG levels [18].

Many studies have shown that, among psychological characteristics, greater coping through positive cognitive reconstruction and problem-focused coping led to higher PTG levels [16,20,22]. Finally, greater social support is consistently reported to be correlated with higher PTG levels [12,20,23].

Therefore, the objective of this study was to measure PTG levels in HSCT survivors and to investigate factors related to PTG.

## Methods

### Procedure and participants

Research participants were adult HSCT patients from the ambulatory setting of Hospital A, a tertiary hospital in Seoul, Korea, who met the selection criteria and provided consent to participate. Detailed selection criteria included (1) at least 18 and less than 65 years old, (2) within 5 years since receiving allogeneic HSCT, and (3) Eastern Cooperative Oncology Group Grade 2 or less, that is, able to move and carry out activities of daily living. Exclusion criteria included (1) second HSCT, (2) persistent need for blood transfusion after transplantation, and (3) patients with GVHD Grade 3 or more. Following approval from the Institutional Review Board, the data were collected for 10 weeks, from April to June of 2012. A paper questionnaire was provided at the outpatient clinic, and responses were collected immediately.

During the study period, a total of 105 patients met the selection criteria and were invited to participate. Of these, four patients did not consent to participate, and one did not complete the survey; thus, the final number of participants was 100.

## Measures

### Post-traumatic growth

The Korean version of the Post-traumatic Growth Inventory (PTGI), developed by Tedeschi and Calhoun [5,8], was used to measure PTG levels. Positive changes perceived by individuals after experiencing traumatic events were measured on a six-point Likert scale with higher total scores meaning more positive changes. The 21 items consist of five subcategories: new possibilities, relating to others, personal strength, appreciation of life, and spiritual change. Reliability and validity were established in South Korea with university students, the general public, military personnel, and post-traumatic stress disorder patients [8]. The internal consistency for PTGI was Cronbach's  $\alpha$  0.92, and Cronbach's  $\alpha$  of the subcategories were 0.83 or greater. The internal consistency in this study was found to be high also, with Cronbach's  $\alpha$  0.96.

### Evaluation of trauma

The Impact of Event Scale—Revised (IES-R) was used for trauma evaluation. The 22-item IES-R was designed by Weiss and Marmar to assess hyper-arousal, intrusion, and avoidance [24]. The IES-R is scored on a five-point Likert scale, with higher scores signifying more severe traumatic events. The Korean version, validated with university students and admitted patients [25], was used. Cronbach's  $\alpha$  values were reported from 0.79 to 0.90 in

original development, 0.83 in Korean adaptation, and 0.88 in this study.

### Social support

Blumenthal and colleagues' Perceived Social Support Scale was used to evaluate social support from family, friends, and other important individuals [26]. It has 12 items in total and uses a seven-point Likert scale with higher scores meaning higher levels of social support. The Korean version [12] had high internal consistency, with Cronbach's  $\alpha$  value of 0.92, which was also identical in this study.

### Support from healthcare professionals

To evaluate the level of support from healthcare professionals, we utilized 12 items from Kim's Social Support Scale, revised and supplemented by Shin [27]. Items were rated on a five-point Likert scale. Internal consistency was good with Cronbach's  $\alpha$  0.94 at development [27] and in this study also.

### Demographic and clinical variables

The following socio-demographic characteristics were also surveyed: properties related to transplantation such as age at time of transplantation, diagnosis, donor, and post-transplantation re-hospitalization experience and cause, usage of and reasons for post-transplantation nurse counseling, and opinions on additional content needed for post-transplantation education.

### Data analysis

Data analyses were conducted using SPSS version 18.0 for Windows. Frequency analysis and cross-analysis were conducted to analyze general characteristics, and an independent *t*-test was conducted to analyze gender differences. Correlation analysis was performed to determine whether general characteristics, disease-related characteristics, social support, and traumatic event stress intensity were related to PTG; correlations between the variables confirmed to be correlated with PTG were also examined. Lastly, using the variables showing correlation to PTG, regression analysis was conducted to evaluate their predictive power for PTG. Statistical significance level was set to  $p < 0.05$ .

## Results

### Demographic information and clinical characteristics

The average age was 41.07 years with a similar ratio of men and women; 63% indicated they participated in religion, and, although there was no difference in religion type by gender, women had statistically significant higher frequency of religious activities than men ( $t=2.23$ ,  $p=0.03$ ). In terms of economic status, 41 participants found both medical and

living expenses to be burdensome; this comprised the largest portion. Diagnosis of acute myeloid leukemia was most prevalent, and the average length of time since transplantation was 31.35 months (Table 1).

### Characteristics of PTG, trauma impact, and social support

The PTG level for men and women were 61.02 and 73.07, respectively. Women's scores were statistically significantly higher overall ( $p=0.01$ ), as well as for all PTG subcategories except for 'new possibilities'.

The total score for traumatic impact was also statistically significant higher in women (19.59) than in men (14.55) ( $t=-2.14$ ,  $p=0.04$ ). Among the subcategories, 'avoidance' and 'hyper-arousal' displayed no gender difference, but 'intrusive thinking', a subcategory that re-

**Table 1.** Demographic information and clinical variables (N = 100)

Variable	N = 100
Age (years)	
M $\pm$ SD	41.07 $\pm$ 12.39
Range	19–61
Gender	
Men	56
Women	44
Marital status	
Married	61
Never married	39
Education	
Middle school or less	11
Completed high school	46
College educated or graduate degree	43
Perceived financial burden	
Both living and medical expenses burden	41
Only medical expenses burden	29
No expense burden	30
Frequency of religious activities	
Over 1/week	23
Over 1/month	9
Over 1/year	31
Never	37
Time since transplant (months)	
M $\pm$ SD	31.35 $\pm$ 13.8
Range	12–60
Donor	
Sibling	48
Parent or child	15
Unrelated	37
Post-transplant nurse counseling	
Yes	73
No	27
Diagnosis	
AML	52
ALL	19
MDS	13
SAA	12
NHL ect.	4

AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; MDS, myelodysplastic syndrome; SAA, severe aplastic anemia; NHL, non-Hodgkin's lymphoma.

flects repeated thoughts about the event, was statistically significant higher in women. Responses that measured 'intrusive thinking' were 'I keep thinking about the stem cell transplantation even when trying not to', 'I have dreams about the stem cell transplantation, and 'things that remind me of stem cell transplantation trigger emotions at the time as the transplantation.' The total scores for social support were significantly higher in women (70.78) compared with men (63.75) ( $t = -2.75$ ,  $p = 0.01$ ); however, there was no difference by gender for support from healthcare professionals (Table 2).

### Relations between PTG and demographic and clinical characteristics

Correlation analysis was conducted to examine the relations between PTG levels and general characteristics. Greater frequency of religious activities was correlated with higher PTG levels ( $r = 0.27$ ,  $p = 0.01$ ), and higher education levels with higher PTG levels ( $r = 0.21$ ,  $p = 0.03$ ), both at statistical significant levels. Further, statistically significant higher PTG levels were found in those who utilized post-transplantation nurse counseling ( $r = 0.26$ ,  $p = 0.01$ ). Other characteristics, such as age, economic status, time since transplantation, re-hospitalization, hospitalization due to host responses, marital status, and graft types, were not found to be statistically significantly related to PTG (Table 3).

### Relations among PTG, trauma impact, and social support

To examine the relationships among PTG, trauma evaluation, perceived social support, and support from healthcare professionals, correlation analysis was performed. The results showed only 'intrusive thinking', a subcategory of event impact, to be related to total PTG score ( $r = 0.23$ ,  $p = 0.02$ ). Social support was highly related

**Table 2.** Characteristics of PTG, trauma impact, and social support

Variables	Possible range	M (SD) Men	M (SD) Women	t
PTGI	0–105	61.02 (25.20)	73.07 (18.10)	–2.78**
Appreciation of life	0–15	6.91 (2.68)	8.02 (2.00)	–2.37*
Relating to others	0–35	19.70 (9.13)	23.57 (6.66)	–2.45*
New possibilities	0–25	18.34 (7.56)	20.70 (5.54)	–1.81
Personal strength	0–20	12.13 (5.12)	14.80 (3.55)	–3.08**
Spiritual change	0–10	3.95 (3.11)	5.98 (3.07)	–3.26**
IES-R	0–88	14.55 (11.41)	19.59 (12.01)	–2.14*
Avoidance	0–32	5.98 (5.49)	6.66 (6.50)	–0.56
Hyper-arousal	0–24	4.32 (3.93)	6.00 (4.70)	–1.94
Intrusion	0–32	4.25 (4.24)	6.93 (4.89)	–2.93**
PSSS	12–84	63.75 (13.60)	70.78 (11.50)	–2.75**
HP's support	12–60	47.07 (9.19)	49.41 (7.17)	–1.39

PTGI, Post-traumatic Growth Inventory; IES-R, Impact of Event Scale revised; PSSS, Perceived Social Support Scale; HP, healthcare professionals.

\* $p < 0.05$ .

\*\* $p < 0.01$ .

**Table 3.** Intercorrelations among study variables

Variables	PTG	IES-R total	Intrusive thinking	Social support	HPs' support	Age
PTG	–					
IES-R total	0.131	–				
Intrusive thinking	0.232*	0.822**	–			
Social support	0.538**	0.032	0.051	–		
HPs' support	0.522**	0.175*	–0.036	0.478**	–	
Age	0.035	0.042	0.049	–0.242**	–0.005	–
Religious activity	0.266**	0.108	–0.148	–0.088	0.002	–0.050
Education level	0.214*	0.024	–0.111	0.313**	0.167	–0.255**
Financial burden	0.062	0.073	–0.105	0.106	0.140	–0.174
Counseling	0.264**	0.115	0.007	–0.001	–0.056	–0.104

PTG, post-traumatic growth; IES-R, Impact of Event Scale—Revised; HP, healthcare professionals.

\* $p < 0.05$ .

\*\* $p < 0.01$ .

with total PTG score ( $r = 0.54$ ,  $p < 0.001$ ), and support from healthcare professionals ( $r = 0.52$ ,  $p < 0.001$ ) was also seen to be highly related (Table 3).

### Variables predicting post-traumatic growth

To identify the variable that best explains PTG, multiple regression analysis by input method was conducted. Education level, frequency of religious activities, utilization of nurse counseling, intrusive thinking from impact of event scale, social support, and support from healthcare professionals were all confirmed to have statistically significant relations with PTG. Further, as PTG level, trauma evaluation, and social support showed statistically significant gender differences, gender was also included in the analysis. The results demonstrated that the regression model was significant ( $F = 15.44$ ,  $p < 0.001$ ) with explanatory power of 50.5%. Support from healthcare professionals ( $\beta = 0.35$ ,  $p < 0.001$ ) was identified as having the biggest influence on PTG in HSCT patients, followed in order of power of influence by social support ( $\beta = 0.31$ ,  $p = 0.001$ ), utilization of nurse counseling ( $\beta = 0.26$ ,  $p = 0.001$ ), intrusive thinking ( $\beta = 0.21$ ,  $p = 0.01$ ), and frequency of religious activities ( $\beta = 0.19$ ,  $p = 0.01$ ). There was no multicollinearity (Table 4).

### Discussion

In HSCT survivors, a high level of PTG is proposed to be an average score greater than 64 points [14]. In this study, the average total PTG score in allogeneic HSCT patients was 66.32, with women showing statistically significantly higher levels (73.03) than men (61.02). The results were similar to those from previous studies conducted outside of South Korea on HSCT patients [14–17] and those conducted on Korean breast cancer patients [12,13]. The level was higher than PTG scores in patients with cancers of poor prognosis, such as lung, head, and neck cancers [14].

The results indicating PTG levels to be higher in women and in those with more frequent religious

**Table 4.** Multiple regression analysis for variables predicting post-traumatic growth

Variables	B	SE	$\beta$	t	Adj. R <sup>2</sup>	F
F	-67.85	15.10		-4.49	0.505	15.44**
Gender	0.51	3.66	0.01	0.14		
Frequency of religious activities	3.73	1.46	0.19	2.56**		
Education	3.48	2.40	0.11	1.45		
Post-transplantation counseling	13.22	3.73	0.26	3.54**		
IES-R: intrusive thinking	1.04	0.37	0.21	2.84**		
Social support	0.54	0.15	0.31	3.52**		
HPs' support	0.96	0.22	0.35	4.31**		

IES-R, Impact of Event Scale—Revised; HP, healthcare professionals.

\* $p < 0.05$ .

\*\* $p < 0.01$ .

activities support previous study findings. However, multiple regression analysis showed that gender did not have a significant relation to PTG. This may be reflective of the fact that PTG-related factors, such as social support, pursuit of religion, and intrusive thinking over traumatic events, are relatively higher in women than in men, as indicated in the bivariate analysis. Although education level was not shown to be a related factor for PTG, this was a highly educated group, with 89% of participants with education levels of high school or higher, which is typical in Korea.

In addition, level of event impact and PTG did not show statistically significant correlations. Despite this, the 'intrusive thinking' subcategory had a positive correlation with PTG and was higher in women. This supports the PTG theory and findings from previous studies that transplant-related ruminations in HSCT patients precede transformative reflection, which can, in turn, facilitate PTG [9,28,29]. Although rumination can accompany negative psychological symptoms, PTG is developed in the same context as Post-traumatic Stress Syndrome (PTSS) [5]. Even in the PTG model, the early stages of an event can have repetition of automatic negative thoughts, and such negative ruminations are known to be related to psychological distress, such as depression and anxiety [28]. However, in the PTG model, negative rumination does not remain in the early stage but extends to find constructive and positive thoughts about the event through elaboration of thought. Expressive writing can motivate patients and allow them to find meaning in the event before consolidating the event experience through cognitive restructuring [9]. Thus, recommending expressive writing on experiences after allogeneic HSCT can be a useful method to facilitate PTG.

The cut-off point for PTSS has been proposed as 25 points in the Korean version of the IES-R [25]. Although this study did not show significant relations between total event impact score and PTG, about 20% of the participants (9 men and 10 women) exceeded the cut-off point, showing indications of possible PTSS. However,

considering the fact that the participants were in relatively good condition after completing treatment, there is a greater possibility of PTSS following HSCT in patients at large, which is a challenge for healthcare professionals as to how this can be transformed into a more positive perception, such as PTG.

A limitation in this study was that patients who experienced severe GVHD or infections were excluded from the recruitment in evaluating PTG for HSCT patients. Although accurate comparisons are difficult, it can be assumed that those with little or no GVHD were included as study participants, which may also have resulted in differences in PTG from the population.

There was also a limitation with uneven recruitment for age, which can influence the finding that age was not related to PTG. As HSCT is also performed on young children, future studies comparing PTG levels of patients aged 10–19 years to those of patients aged 30–59 years, who constituted the majority in this study, would allow better understanding of the relationship between PTG of HSCT patients and age.

Danhauer and colleagues stated in their longitudinal study of PTG in leukemia patients that PTG levels increased with passing of time since transplantation [19]. As the participants of this study were already diagnosed with severe blood cancers or diseases, longitudinal examination of PTG tendencies during treatment is needed to analyze the influence of related factors.

This study did not measure event-related psychological symptoms such as depression and anxiety. There are reports that depression and anxiety do not change considerably over time, such as a prior study with 236 HSCT patients that reported approximately 25% exhibited depression and anxiety roughly 3 years following transplantation, which was at similar levels as time of diagnosis [30]. The mean time since transplantation was 31 months, and it can be assumed that participants had some degree of psychological distress. Although unidentified distress level in participants was a limitation in this study, the measurement for level of event impact included items that were conceptually similar to depression and anxiety. Prior studies investigating the relationships among depression, anxiety, or distress and PTG do not show consistent results [16,31], but this was not the primary purpose of this study, and may be considered for future study.

### Clinical implication

This study highlights focus areas to facilitate PTG in patients following HSCT. Interventions to promote PTG in allogeneic HSCT patients, such as reinforcing social support and support from healthcare professionals, along with encouraging re-evaluation of the event and counseling utilization can be used in practice. Possible methods to strengthen support from healthcare professionals include proactive counseling, forming support groups, and attending

meetings as an advisor. In previous studies, cognitive-behavioral therapy and mindfulness-based stress reduction programs were both effective to facilitate PTG [13,32,33]; these programs can be recommended. To encourage conceptualization and re-evaluation of the event, narrative writing can be helpful, as well as creative activities such as art therapy to help with emotional expression and self-reflection [34]. These supportive efforts may need to be especially tailored to male patients, as they appear to have greater need in terms of PTG.

This study found a positive relation between PTG and post-HSCT counseling from nurses. Providing accurate fact-based information instead of information of questionable background or source and contact information for counseling to receive support from health care professionals are ongoing needs. Identifying problems and counseling via phone calls following discharge after transplantation can also facilitate encounters for post-HSCT counseling and enhancing PTG.

## Conclusions

This study aimed to provide basic data for developing interventions to enhance PTG in allogeneic HSCT patients by analyzing PTG and related factors. In this study, support from healthcare professionals, social support, utilization of nurse counseling, reflective thinking about the transplantation, and level of religious activities were identified as factors related to PTG in HSCT patients. Although this study also found differences in PTG level based on gender, regression analysis found no significance, which suggests the role of gender needs to be further examined.

On the basis of this study's results, to enhance PTG in HSCT patients, programs that enhance support from healthcare professionals and social support, along with expansion of nurse counseling are needed. Furthermore, support groups, expressive writing, cognitive-behavioral therapy, and meditation, among others, can serve as methods to enhance PTG.

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