

Medically Induced Exacerbation of PTSD Following Lung Transplantation: A Case Series

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Abstract

Posttraumatic stress disorder (PTSD) occurs at double the rate in individuals undergoing lung transplantation, compared to the normal population. The psychological sequela of PTSD makes recovery more challenging and may result in poor medical and psychological outcomes. A series of three cases illustrate this presentation. In all cases, PTSD history and symptomatology was undisclosed prior to lung transplantation, despite robust psychological evaluation. All patients experienced traumatic delirium during the acute recovery phase from transplantation. Re-emergence and exacerbation of PTSD symptoms related to remote trauma lasting up to 2 years after transplant. Noncompliance with post-transplant recovery occurred in the sample of cases presented. Major surgeries, such as lung transplant may exacerbate premorbid PTSD possibly via psychological sequela such as delirium, regardless of type or remoteness of trauma experiences. Existing psychological evaluation practices may not be adequate to capture PTSD as many patients may fail to disclose relevant history. Novel evaluation and treatment methods need to be developed.

Keywords

Posttraumatic stress
Transplantation
Lung transplantation
Delirium

Introduction

Posttraumatic stress disorder (PTSD), a debilitating psychological condition triggered by experiencing or witnessing a traumatic event such as the threat of death, serious injury, or sexual violence, that is associated with intrusive thoughts, avoidance of trauma reminders, worsening cognition and mood, and marked alterations in arousal and reactivity (American Psychiatric Association, 2013), occurs at double the rate in lung transplant recipients (12–15% prevalence) (Gries et al., 2013) compared to the general population (Kessler et al., 2005). The increased prevalence of PTSD in lung transplant recipients occurs despite data to suggest a history of childhood trauma is high, but comparable between lung transplant candidates (24.2%) (Kennedy, Zubair, Clark, & Jowsey-Gregoire, 2016) and the general population (20–50%) (Springer, Sherida, Kuo, & Carnes, 2003). Past studies have indicated patients undergoing lung transplantation may be at higher risk for developing PTSD due to the (1) psychological distress of having life-threatening lung disease and transplant surgery, (2) intensive care unit (ICU) stay with increased risk of medical trauma and/or delirium, and (3) lifelong fear of rejection, and ultimately, death (Davydow, Lease, & Reyes, 2015; Gries et al., 2016). The exposure to post-transplant medical trauma in combination with delirium may trigger or exacerbate symptoms of PTSD. In fact, post-surgical delirium, characterized by acute disturbance in attention and cognition, has been documented in as many as 37% of lung transplant recipients (Anderson et al., 2018). Lung transplant recipients may have greater risk for delirium because of medical sequelae uniquely resulting from transplantation, such as lower mean intra-operative cerebral perfusion pressure and primary graft dysfunction (Smith et al., 2016). However, the impact of a pre-existing history of trauma exposure and PTSD on post-transplant recovery is less clear.

We present three illustrative cases of transplant patients who, in the immediate and acute post-transplant phase of treatment, experienced robust symptoms of PTSD predating their lung transplantation and lung disease history. Notably, no trauma history was disclosed during an intensive pre-transplant psychological work-up. These cases suggest that (1) exposure to anesthesia and high-dose steroids, commonly used in lung transplantation, particularly can result in delirium and trigger new or exacerbate latent PTSD, (2) history of trauma and resulting PTSD may be difficult to discover by transplant teams, even with robust psychological evaluation, (3) the remoteness of incident trauma and resulting PTSD, despite stable presentation, may not decrease the risk of adverse outcomes following lung transplantation.

Case 1

“Ms. A” was a 69-year-old woman who received a single-lung transplant for interstitial lung disease. She had no known psychiatric history prior to transplant and was identified as a good transplant candidate psychologically. She was referred to the psychology team 2 months following her transplant, while she was in the ICU, due to refusal to participate in physical therapy or use her bi-level positive airway pressure device at night, resulting in hypoxia. Ms. A initially denied psychological difficulties underlying her behavior and attributed her poor compliance and irritability to uncontrolled pain. She was hospitalized for over 5 months following lung transplantation, mainly because of lack of progress towards physical therapy goals due to noncompliance.

Following discharge, Ms. A disclosed to the transplant psychologist her experience of severe delirium for 3 days following her lung transplantation, in which she thought she was in the Vietnam War constantly running from enemy soldiers, which was extremely traumatic for her. Upon further query, she acknowledged she had a history of childhood abuse, however, she declined to give further details, as she found memories of her trauma too disturbing to discuss. She endorsed a significant increase in flashbacks to her original trauma in the months following her transplant and acknowledged that these flashbacks impacted her ability to adequately participate in physical therapy while hospitalized. Ms. A attributed her noncompliant behavior while admitted post-transplant to this combination of post-transplant delirium and worsening PTSD from childhood abuse. She refused treatment for her PTSD symptoms, even after

appropriate diagnosis, as she did not feel ready to discuss her trauma, and made minimal gains in her progress with physical therapy over the 2 months following her disclosure of PTSD symptoms.

Case 2

“Ms. B” was a 57-year-old woman who received a bilateral lung transplant for pulmonary fibrosis. No significant psychological concerns were noted by the transplant team. Two years after her transplant, she was referred to transplant psychology due to a depressed mood and sudden weight gain. Ms. B reported her initial post-transplant course included severe delirium in which she thought she had witnessed her nurse and doctor having an affair and plotting to kill her by giving her an overdose of medication. Looking back on her experience with delirium, she stated: “I know it didn’t happen, but I can remember it like it did. Even to this day, I can see everything clearly.”

Ms. B also revealed she is a survivor of multiple rapes, which occurred during adolescence. Consequently, she experienced severe untreated PTSD symptoms in her early adulthood. Ms. B stated she thought she had recovered from her PTSD prior to transplant and did not think it was relevant to inform the team of her trauma history. She reported that her post-transplant delirium reminded her of her past traumas, as she felt a similar lack of control. Mrs. B’s undisclosed and untreated PTSD likely increased her susceptibility to traumatic and persecutory delirium content, and the delirium context likely exacerbated her PTSD symptoms. She reported lingering feelings of guilt related to her traumas and delirium. Ms. B reported continuing to be bothered by her delirium years after transplant.

Ms. B received a brief course of modified cognitive processing therapy for her remaining PTSD symptoms at the time of referral. She also opted to become involved with activism events for women’s rights issues and to discuss her history of sexual trauma and its impact on her wellbeing with friends and family. Her symptoms resolved in 2 months and she made significant gains in compliance with dietary and exercise recommendations.

Case 3

“Mr. C” was a 69-year-old male who underwent bilateral lung transplant for

pulmonary fibrosis. No major concerns were noted by psychology prior to transplant. He served in the Navy during the Vietnam War, but initially denied being exposed to combat trauma during his service. During his initial post-transplant hospitalization, he requested psychological services for delirium and nightmares that he attributed to PTSD. Mr. C revealed that during the war, he was stationed on a boat that overlooked a battlefield on which he saw soldiers dying “all day every day for 6 months.” Mr. C stated that in the 3 days following transplant, he experienced intense delirium, consisting of a continuous flashback to his service in the Vietnam War. He reported seeing uniformed soldiers in his hospital room for several weeks following transplant and experiencing frequent nightmares related to his combat trauma.

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Mr. C also reported a secondary trauma in which he learned his son had been arrested for sexually abusing Mr. C’s granddaughter. In addition to his re-experiencing symptoms of combat trauma during hospitalization, Mr. C reported an increase in guilt related to his son’s molestation of his granddaughter, which he attributed to the limited time they spent together as his son was maturing due to Mr. C’s deployments and estrangement from his son’s mother.

He denied having experienced trauma during his pre-transplant psychological evaluation because he was concerned his family, who was not aware of his prior exposure to trauma, would be upset. Mr. C’s active PTSD symptoms likely also contributed to his significant medically unexplained pain management problems during his hospitalization, which worsened with increased PTSD symptoms and limited his progress in physical therapy, thus delaying his discharge by several weeks. His PTSD symptoms and pain management problems ceased following a modified course of Cognitive Processing Therapy that was administered during his hospitalization (Table 1).

Table 1

Trauma type and outcome

Patient	Type of trauma	Remoteness of trauma exposure	ICU delirium	Disclosure prior to transplantation	Intervention & response
A	Childhood abuse	50+ years	Yes	No	Declined, symptoms and

Patient	Type of trauma	Remoteness of trauma exposure	ICU delirium	Disclosure prior to transplantation	Intervention & response
					compliance did not improve
B	Sexual trauma	40+ years	Yes	No	Modified CPT, symptoms and compliance problems remitted
C	Combat	30+ years	Yes	No	Modified CPT, symptoms and compliance problems remitted

Discussion

PTSD has been under-recognized as common element in lung transplantation, but awareness of PTSD that is exacerbated during the transplant process is increasing (DiMartini, Dew, Kormos, McCurry, & Fontes, 2007). Risk of developing PTSD to subsequent trauma increases when there is a history of prior trauma (Breslau, Peterson, & Schultz, 2008). PTSD in the post-acute period of lung transplantation may be a cumulative effect of possible prior trauma combined with medical trauma in the context of medications and anesthesia contributing to a state of delirium. Consequently, when patients with a history of PTSD symptoms are exposed to delirium-inducing medications and procedures which may cue latent memories, even patients that appeared to be stable or coping adequately with remote traumas may be ill-equipped to psychologically handle the demands of recovery from lung transplantation. This combination is likely a contributing factor to the doubled prevalence of PTSD in lung transplant recipients compared to the general population.

The symptoms of active PTSD include extreme anxiety, hypervigilance, agitation, social withdrawal, avoidance of trauma reminders, and insomnia, which have been shown to worsen morbidity and mortality following heart transplant (Favaro et al., 2011), are yet unstudied in lung transplant. Given that the course of untreated PTSD is often chronic, exacerbations may continue to impact the transplant recovery process, manifesting themselves in medical

noncompliance, physical deconditioning, or poor quality of life.

The cases presented illustrate poor disclosure of trauma history and PTSD symptoms during transplant work-ups. The psychological evaluation for lung transplantation at this institution includes, at minimum, a 60-min psychological interview with a PhD level psychologist which explicitly inquires about both previous exposure to traumatic experience as well as lifetime symptoms of PTSD. Some patients avoided disclosing trauma exposure and PTSD not only to the transplant team, but also their family members and caregivers. In instances where caregivers were aware of previous trauma, they did not disclose it to the transplant team. Poor disclosure may be due to a constellation of causes including (1) patient's lack of awareness/insight, (2) motivation to appear psychologically stable during evaluation process/obtain transplant, (3) inadequate inquiry/inappropriate evaluation methods by the transplant team, (4) greater severity of avoidance symptoms. To address these barriers, transplant candidates must be provided with specific psychoeducation on both the nature of PTSD symptomatology and possible ill effects on transplant outcomes. Subsequently, affected candidates must be offered effective evidence-based treatments, such as cognitive processing therapy, trauma-focused cognitive behavioral therapy, narrative exposure therapy, eye movement desensitization and reprocessing, or prolonged exposure therapy (Morkved et al., 2014; Resick, Monson, & Chard, 2016; Seidler & Wagner, 2006), to address their PTSD. Because social desirability is at play in candidate's disclosure patterns regarding PTSD, standardized evaluation methods that include validity indices, such as the Minnesota Multiphasic Personality Inventory-2 Restructured Form (Tellegen et al., 2003) may need to be employed. Transplant teams must be cognizant of both the high prevalence of PTSD, its resulting risk factors, and patient's reluctance to disclose.

Studies have documented that patients found to be at highest risk for developing PTSD have a tendency to be younger, without private insurance, diagnosed with bronchiolitis obliterans syndrome, and more likely to have pulmonary fibrosis than chronic obstructive pulmonary disease. They were also more likely to report arousal and re-experiencing symptoms, characteristic of PTSD (Dew et al., 2012). Moreover, childhood physical or sexual abuse survivorship was common in 24.2% of lung transplant recipients and associated with decreased survival (Kennedy et al., 2016). Consequently, remote trauma exposure might affect

physiological stress reactivity, neuronal changes (Gould & Tanapa, 1999) or brain development, altogether, if exposure is early enough in life (Perry & Pollard, 1998), all of which could result in maladaptive coping and place one at increased risk for psychiatric morbidity. Thus, these known risk factors should inform the psychological evaluation process to better identify individuals with PTSD. Psychological intervention and psychiatric consultation should be readily available in the ICU and inpatient units during the post-acute period to provide early intervention when PTSD symptoms emerge. Given the high prevalence rate of PTSD in lung transplant recipients, post-transplant routine screening may be indicated at 1 week, 1, 3, 6, and 12 months intervals.

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All presented cases experienced delirium following lung transplantation. Delirium induced by medical interventions, in the post-acute phase may be a risk factor for PTSD exacerbation. Risk factors for delirium should, of course, be minimized when possible by the transplant team. Those experiencing delirium with known trauma history or PTSD should be closely monitored for PTSD exacerbation. All patients with delirium but without known trauma or PTSD history, should still be evaluated for signs of PTSD given a tendency for poor disclosure. Noncompliance with medical treatment should also be a trigger for PTSD screening in this population, as it is often a visible indicator of psychological complications. Further study of lung transplant candidates is indicated to better understand how pre-existing PTSD symptoms are exacerbated by delirium and what strategies are most effective at mitigating these risks to minimize deleterious effects on morbidity and mortality.

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Compliance with Ethical Standards

Conflict of interest Yelena Chernyak and Lisa Teh declare that they have no conflict of interest.

References

- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Association.
- Anderson, B. J., Chesley, C. F., Theodore, M., Christie, C., Tino, R., Wysoczanski, A.,... Diamond, J. M. (2018). Incidence, risk factors, and clinical implications of post-operative delirium in lung transplant recipients. *Journal of Heart and Lung Transplantation, 37*, 755–762.
- Breslau, N., Peterson, E. L., & Schultz, L. R. (2008). A second look at prior trauma and the posttraumatic stress disorder effects of subsequent trauma. *Archives of General Psychiatry, 65*(4), 431–437.
- Davydow, D. S., Lease, E. D., & Reyes, J. D. (2015). Posttraumatic stress disorder in organ transplant recipients: A systematic review. *General Hospital Psychiatry, 37*, 387–398.
- Dew, M. A., DiMartini, A. F., Dabbs, A. D., Fox, K. R., Myaskovsky, L., Posluzny, D. M.,... Toyoda, Y. (2012). Onset and risk factors of anxiety and depression during the first two years after lung transplantation. *General Hospital Psychiatry, 34*, 127–138.
- Dew, M. A., Kormos, R. L., Roth, L. H., Srinivas, M., DiMartini, A., & Griggith, B. P. (1999). Early post-transplant medical compliance and mental health predict physical morbidity and mortality one to three years after heart transplantation. *Journal of Heart and Lung Transplantation, 18*, 549–562.
- DiMartini, A., Dew, M. A., Kormos, R., McCurry, K., & Fontes, P. (2007). Posttraumatic stress disorder caused by hallucinations and delusions experienced in Delirium. *Psychosomatics, 48*, 5.
- Favaro, A., Gerosa, G., Caforio, A. L. P., Volpe, B., Rupolo, G., Zarneri, D.,... Santonastaso, P. (2011). Posttraumatic stress disorder and depression in heart transplantation recipients: The relationship with outcome and adherence to medical treatment. *General Hospital Psychiatry, 33*, 1–7.

Gould, E., & Tanapa, T. (1999). Stress and hippocampal neurogenesis. *Biological Psychiatry*, 46(11), 1472–1479.

Gries, C. J., Dew, M. A., Curtis, J. R., Edelman, J. D., Dabbs, A. D., Pilewski, J. M.,... White, D, B. (2016). Nature and correlates of post-traumatic stress symptomatology in lung transplant recipients. *Journal of Heart Lung Transplantation*, 32, 525–532.

Kennedy, C. C., Zubair, A., Clark, M. M., & Jowsey-Gregoire, S. (2016). Childhood abuse is associated with worse survival following lung transplantation. *Progress in Transplantation*, 26(2), 178–182.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Marikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey replication. *Archives of General Psychiatry*, 62, 593–602.

Morkved, N., Hartmann, K., Aarsheim, L. M., Holen, D., Milde, A. M., Bornyea, J., & Thorp, S. R. (2014). A comparison of narrative exposure therapy and prolonged exposure therapy for PTSD. *Clinical Psychology Review*, 34(6), 453–467.

Perry, B. D., & Pollard, R. (1998). Homeostatis, stress, trauma, and adaptation: A neurodevelopmental view of childhood trauma. *Child Adolescent Psychiatry Clinics of North America*, 7(1), 33–51.

Resick, P. A., Monson, C. M., & Chard, K. M. (2016). *Cognitive processing therapy for PTSD: A comprehensive manual*. New York: Guilford Press.

Seidler, G. H., & Wagner, F. E. (2006). Comparing the efficacy of EMDR and trauma-focused cognitive behavioral therapy in the treatment of PTSD: A meta-analytic study. *Psychological Medicine*, 36(11), 1515–1522.

Smith, P. J., Blumenthal, J. A., Hoffman, B. M., Rivelli, S. K., Palmer, S. M., Davis, R. D., & Mathew, J. P. (2016). Reduced cerebral perfusion pressure during lung transplant surgery is associated with risk, duration and severity of postoperative delirium. *Annals of American Thoracic Society*, 13, 180–187.

Springer, K. W., Sherida, J., Kuo, D., & Carnes, M. (2003). The long-term health outcomes of childhood abuse. An overview and a call to action. *Journal of General Internal Medicine, 18*(10), 864–870.

Tellegen, A., Ben-Porath, Y. S., McNulty, J. L., Arbisi, P. A., Graham, J. R., & Kaemmer, B. (2003). *MMPI-2 restructured clinical (RC) scales: Development, validation, and interpretation*. Minneapolis: University of Minnesota Press.