

Review

Psychological factors and immune–inflammatory mechanisms in cancer-related organ transplantation: Toward a multimodal integrative framework

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Abstract: Cancer patients who undergo organ transplantation after oncologic treatment experience complex biological and psychological stressors that jointly influence immune recovery and graft function. Psychological distress—particularly anxiety and depression—activates neuroendocrine and autonomic pathways that modulate cytokine release, inflammation, and immune tolerance. Evidence from psycho-oncology and transplantation studies demonstrates that heightened distress and low resilience correlate with increased interleukin-6, tumour necrosis factor- α , and C-reactive protein levels, impaired cellular immunity, and delayed post-operative recovery. This review integrates current findings from psychoneuroimmunology, transplantation medicine, and behavioural oncology to elucidate how donor characteristics, perfusion parameters, and psychosocial factors interact to shape outcomes in cancer-related transplantation. Routine psychological assessment using validated instruments such as the Hospital Anxiety and Depression Scale (HADS), together with early interventions—cognitive-behavioural therapy, mindfulness-based stress reduction, and resilience training—may reduce inflammatory activity and improve recovery trajectories. Furthermore, emerging multimodal and machine-learning-assisted analytic approaches provide opportunities for personalised psychosocial care and risk stratification. Understanding these psych neuroimmune interactions supports the development of integrative, precision-based rehabilitation strategies within the scope of psycho-oncology.

Keywords: Anxiety; cancer; HADS; inflammation; psychoneuroimmunology; resilience; stress; transplantation

1. Introduction

Organ transplantation is one of the most demanding and life-sustaining procedures in contemporary medicine. It provides the only curative option for many patients with end-stage organ failure who would otherwise face irreversible deterioration and poor quality of life. Advances in microsurgical techniques, organ preservation, and immunosuppressive therapy have markedly improved both graft survival and long-term patient outcomes [1,2]. Yet recovery after transplantation is not a purely physiological process. It involves profound psychological, social, and behavioural adjustments that determine how the recipient adapts to the new organ and to life after surgery. For many patients, the post-transplant period is characterised by fear of rejection, anxiety about dependence on immunosuppressive medication, and uncertainty about the future. When transplantation occurs in patients who have a history of cancer, the process of adaptation becomes especially complex. Individuals

who undergo organ replacement after oncologic treatment, such as nephrectomy for renal carcinoma or hepatic resection for primary liver cancer, must confront the combined effects of chronic inflammation, surgical trauma, and psychological distress [3].

Globally, both cancer incidence and the number of patients eligible for transplantation continue to rise, creating a growing population of individuals living at the interface of oncology and transplant medicine. Cancer and its treatments induce a range of biological and psychological sequelae. Tumour progression, radiotherapy, and chemotherapy provoke inflammatory cascades that extend beyond the tumour microenvironment and affect systemic immunity [4,5]. These physiological changes often persist long after treatment has ended, leaving patients with lingering immune dysregulation, fatigue, and vulnerability to infection. At the same time, the psychological toll of cancer is substantial. The diagnosis evokes fear, uncertainty, and loss of control, while treatment imposes physical suffering and social isolation. Anxiety, depression, and existential distress are among the most prevalent symptoms, affecting nearly half of all cancer survivors according to epidemiological data [6,7]. These symptoms are not merely emotional consequences of illness; they represent measurable stress responses that interact with endocrine and immune pathways. Chronic activation of the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic–adrenal–medullary (SAM) system results in persistent elevations of cortisol, norepinephrine, and epinephrine, which alter cytokine production, suppress cytotoxic T-cell proliferation, and impair natural-killer (NK) cell activity. Such neuroendocrine alterations can delay wound healing, reduce immune competence, and increase susceptibility to infection.

The field of psychoneuroimmunology offers an explanatory framework for these complex interactions between mind and body. 1–3 This discipline investigates how emotional and cognitive processes influence immune regulation through neural and endocrine signalling. Experimental and clinical research has shown that chronic psychological stress can elevate pro-inflammatory cytokines such as interleukin-6 (IL-6), tumour necrosis factor- α (TNF- α), and C-reactive protein (CRP), all of which are biomarkers of systemic inflammation and poor prognosis in cancer patients. 4–7 Sustained stress responses can alter gene transcription patterns in leukocytes, impair DNA repair mechanisms, and disrupt cytokine feedback loops, ultimately affecting the trajectory of recovery after surgery and medical therapy. The accumulated evidence indicates that psychological factors are integral components of disease biology rather than secondary consequences of illness. Recognising this connection has important implications for both cancer care and transplant medicine.

Within transplantation science, immune regulation determines whether a graft is accepted or rejected. Ischemia–Reperfusion injury, donor age, and perfusion quality have been identified as major contributors to delayed graft function (DGF), a complication defined by the need for dialysis within the first post-operative week or by poor early graft performance [8–10]. While these biomedical determinants are well established, the psychosocial dimension of transplantation has received comparatively less attention. Psychological distress, maladaptive coping, and low treatment adherence can adversely affect immune recovery through inflammatory and behavioural mechanisms. Recipients who experience anxiety or depressive symptoms

often exhibit higher levels of IL-6 and CRP and demonstrate poorer medication compliance, both of which contribute to graft dysfunction. Conversely, emotional stability, optimism, and social support have been associated with improved immune regulation, better adherence, and enhanced quality of life after transplantation [11–14]. These findings suggest that the psychological condition of the recipient is a modifiable biological factor with direct consequences for graft success.

When cancer and transplantation coincide, the biological and psychological burden is amplified. Cancer survivors who undergo organ replacement often retain chronic inflammation and immune imbalance from their previous oncologic treatments [1,7]. They must simultaneously cope with the existential anxiety of cancer survivorship and the lifelong demands of transplantation. Many experiences altered body image, feelings of dependence, and guilt toward the donor or donor family. These emotional burdens activate neural circuits related to vigilance and threat perception, which sustain inflammatory signalling and interfere with immune tolerance. In clinical terms, cancer-related transplantation constitutes a model of dual stress in which oncologic inflammation converges with transplant-induced immune activation. The overlap of these two stress systems creates a heightened vulnerability to delayed recovery, infection, and psychosocial maladjustment.

Addressing this dual burden requires an integrative framework that bridges oncology, psychiatry, and immunology. The present review synthesises current evidence on how psychological distress and resilience influence immune and inflammatory mechanisms in cancer-related organ transplantation. It further explores how donor characteristics, perfusion factors, and psychosocial domains interact within a multimodal conceptual model and discusses the clinical implications for psycho-oncological and transplant rehabilitation. By adopting a biopsychosocial perspective, this work emphasises that psychological assessment and intervention are essential to biological recovery and long-term survival, and should be embedded as standard components of integrative care for patients undergoing cancer-related organ transplantation.

2. Psychological factors and immune–inflammatory mechanisms

2.1. Neuroendocrine and cytokine pathways

Psychological stress triggers a coordinated neuroendocrine cascade that affects nearly every level of immune function. Activation of the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic–adrenal–medullary (SAM) system releases glucocorticoids and catecholamines that reshape leukocyte activity [15,16]. These mediators alter cell trafficking, suppress natural-killer (NK) cell cytotoxicity, and shift cytokine secretion toward a pro-inflammatory profile that favours disease progression. [17]. Persistent cortisol exposure also induces glucocorticoid receptor resistance, which blunts anti-inflammatory feedback and maintains low-grade inflammation. Meta-analytic evidence confirms that chronic stress suppresses cellular immunity and elevates systemic inflammatory markers such as IL-6, CRP, and TNF- α . [4]. Classic laboratory studies demonstrated that acute stress delays wound healing, providing direct behavioural–immune evidence in humans [5].

Neuroimmune communication operates bidirectionally. Cytokines such as IL-1 β , IL-6, and TNF- α send afferent signals to the central nervous system, altering hypothalamic and limbic circuits that regulate mood and motivation [18]. Conversely, cortical appraisal of threat or safety modulates peripheral cytokine release through autonomic outflow. This reciprocal regulation underpins the psychoneuroimmunology model linking emotion and biological recovery. Modern imaging studies further reveal that heightened amygdala reactivity during stress correlates with peripheral inflammation, suggesting that neural vigilance contributes to sustained immune activation. The result is a self-reinforcing cycle: emotional distress enhances inflammatory signalling, which feeds back to the brain to perpetuate anxiety and fatigue. Breaking this loop is therefore a biological as well as psychological imperative in cancer-related transplantation.

2.2. Psychological distress and immune dysregulation in cancer

Within oncology, depressive and anxious states consistently associate with chronic inflammation and diminished antitumour immunity. Elevated IL-6 and CRP predict fatigue, sleep disturbance, and reduced quality of life among breast-cancer survivors [19]. Prospective data show that baseline depressive symptoms precede later cytokine elevations, suggesting a directional relationship rather than simple correlation [20]. At the molecular level, pro-inflammatory transcription factors such as NF- κ B are up-regulated in individuals experiencing long-term distress, while expression of antiviral genes is reduced. This pattern, termed the “conserved transcriptional response to adversity,” contributes to tumour growth and impaired healing.

Perioperative research demonstrates that psychological stress intensifies post-surgical inflammatory cascades. Patients reporting high pre-operative anxiety exhibit greater increases in IL-6 and TNF- α after surgery, slower wound closure, and longer hospitalisation [6]. Such findings have direct implications for transplant settings, where tissue reperfusion injury and immune adaptation occur simultaneously with emotional upheaval. Cancer patients who later require organ transplantation face compounded stressors: residual oncologic inflammation, major surgery, and fear of graft failure. Clinical studies in renal-transplant populations reveal that pre-transplant anxiety and depression correspond with higher post-operative IL-6 and CRP and slower graft recovery [21]. These observations position psychological distress not as a mere symptom but as an active biological determinant influencing immune–inflammatory homeostasis.

The impact extends beyond cytokines. Distress alters autonomic balance by increasing sympathetic tone and reducing vagal activity, which diminishes anti-inflammatory vagal reflexes. Sleep disturbance, appetite loss, and medication non-adherence—common behavioural sequelae of depression—further exacerbate immune dysregulation. Together, these physiological and behavioural mechanisms create a milieu that hinders graft acceptance and accelerates complications. Recognising and treating distress before transplantation may therefore represent a form of immunological pre-habitation that optimises recovery potential.

2.3. Modulation through psychosocial interventions

A growing body of research indicates that psychosocial interventions can recalibrate immune and endocrine activity. Mindfulness-based stress reduction (MBSR) and cognitive-behavioural therapy (CBT) reduce circulating IL-6 and CRP and restore diurnal cortisol rhythm, signalling improved HPA-axis regulation [21,22]. Randomised clinical trials show that CBT-based stress-management training enhances T-cell proliferation and normalises cytokine profiles in women with breast cancer [23]. A comprehensive meta-analysis confirmed measurable increases in NK-cell activity and moderate reductions in pro-inflammatory biomarkers following structured psychological programmes [24]. These effects are biologically meaningful, matching the magnitude of change seen with some pharmacologic anti-inflammatory agents.

The mechanisms underlying these improvements include reduced amygdala activation, enhanced prefrontal regulation of stress appraisal, and strengthened parasympathetic tone. Behavioural strategies such as relaxation training, guided imagery, and mindfulness meditation lower sympathetic output and promote vagal anti-inflammatory signalling. Group-based interventions additionally foster social connectedness, which buffers physiological reactivity to stress. In transplant recipients, early psychological support has been linked to better medication adherence, shorter hospital stays, and improved patient-reported outcomes. Although evidence in cancer-related transplantation remains limited, extrapolation from oncology and transplant psychology suggests that integrating structured stress-management protocols could improve immune recovery and graft adaptation.

Beyond individual therapy, systemic approaches also modulate biological resilience. Interdisciplinary models that embed psycho-oncology within transplant care encourage routine screening for distress and timely referral for intervention. Embedding psychoneuroimmunology principles into clinical pathways can facilitate personalised rehabilitation, allowing clinicians to adjust psychological and medical treatment simultaneously. Such integration reflects a shift from viewing psychological care as ancillary to recognising it as an essential element of physiological recovery. In future, combining psychosocial data with inflammatory biomarkers may enable predictive models that guide both immunosuppressive dosing and behavioural therapy intensity, promoting holistic recovery after cancer-related transplantation.

Figure 1 illustrates the psychoneuroimmunology framework that underpins the relationship between psychological stress, neuroendocrine activation, inflammation, and graft adaptation. Emotional distress activates the hypothalamic–pituitary–adrenal (HPA) axis and sympathetic–adrenal–medullary (SAM) system, releasing glucocorticoids and catecholamines that modulate cytokine profiles (IL-6, TNF- α , CRP). These changes influence immune tolerance and tissue recovery. Conversely, psychological interventions such as cognitive-behavioural therapy (CBT) and mindfulness-based stress reduction (MBSR) can restore homeostasis by reducing neuroendocrine activation and inflammatory tone, thereby supporting graft function and overall recovery.

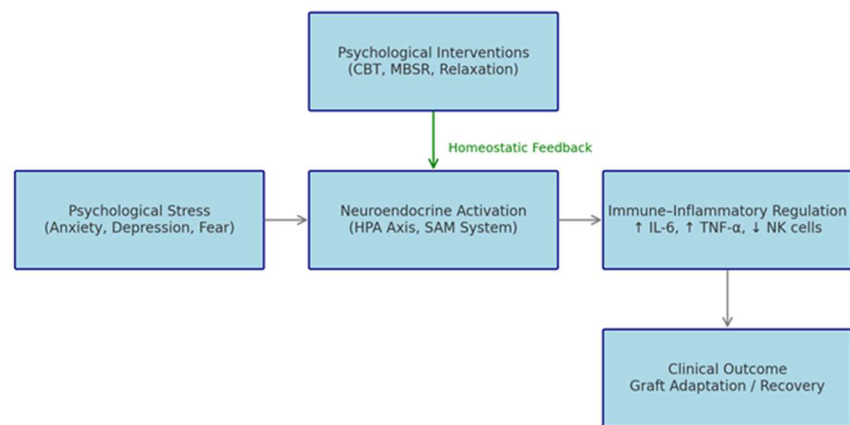


Figure 1. Conceptual framework linking psychological stress, neuroendocrine activation, immune–inflammatory regulation, and graft adaptation.

3. Psychoneuroimmunology in transplantation and cancer recovery

3.1. Psychological stress and graft adaptation

Psychoneuroimmunology (PNI) offers a mechanistic framework for understanding how emotional states shape immune adaptation following transplantation. Chronic activation of the HPA axis and sympathetic pathways heightens inflammatory tone and interferes with immune tolerance, thereby influencing graft survival [25]. Under persistent psychological strain, cortisol and catecholamines circulate at abnormal levels, disturbing the delicate equilibrium between pro- and anti-inflammatory cytokines. This imbalance can reduce regulatory T-cell activity and promote expression of adhesion molecules that attract inflammatory leukocytes to the graft site.

Early investigations in hematopoietic stem-cell transplantation (HSCT) revealed that higher pre-transplant anxiety and depression predicted delayed leukocyte recovery and elevated IL-6 concentrations [12]. Subsequent works extended these observations to solid-organ transplantation, where recipients experiencing sustained distress exhibited higher incidence of acute rejection, greater need for immunosuppressant adjustment, and poorer quality-of-life outcomes [26,27]. These associations underscore that mental distress is biologically embedded in the same regulatory networks that govern graft acceptance.

Klapheke’s foundational review highlighted that psychological stress in transplant candidates augments susceptibility to infection and interferes with adherence to immunosuppressant regimens, indirectly compromising graft outcomes [8]. Modern biomarker and imaging studies confirm that stress-related sympathetic activation increases circulating norepinephrine and alters dendritic-cell antigen presentation, directly linking emotional strain with immune dysregulation [28]. Animal models have shown that experimentally induced stress elevates graft-infiltrating macrophages and accelerates rejection, findings consistent with clinical correlations in human recipients. Collectively, these data demonstrate that the

“psychological climate” surrounding transplantation can exert tangible effects on cellular immunity and tissue integrity.

Beyond immune signalling, stress also affects vascular and metabolic pathways relevant to graft function. Elevated catecholamines increase vasoconstriction and oxidative stress, reducing perfusion and oxygen delivery to transplanted tissue. Hypercortisolaemia alters glucose and lipid metabolism, potentially impairing wound repair and promoting endothelial dysfunction. Together, these neuroendocrine consequences form an integrated biobehavioural mechanism through which emotional distress translates into biological risk.

Table 1 summarises the key psychoneuroimmunology mechanisms through which psychological distress influences immune–inflammatory regulation in cancer-related organ transplantation. Emotional and cognitive states such as anxiety, depression, and perceived loss of control affect hormonal secretion, cytokine signalling, and immune-cell function. These biological changes, in turn, alter graft adaptation and recovery. Understanding these interactions provides a mechanistic foundation for integrating psychological assessment into transplant medicine.

Table 1. Key psychoneuroimmunology mechanisms linking psychological distress and immune regulation in cancer-related transplantation

Psychological factor	Biological mediator(s)	Clinical consequence	Representative evidence (Ref No.)
Anxiety and hypervigilance	↑ Cortisol, ↑ Catecholamines, altered HPA-axis feedback	Increased IL-6, TNF-α; delayed wound healing	[4,5,15–18]
Depressive mood	Dysregulated serotonin–cytokine interaction; ↓ NK-cell activity	Elevated CRP, reduced immune surveillance	[6,19–21]
Chronic perceived stress	Persistent activation of SAM system; glucocorticoid resistance	Sustained low-grade inflammation; impaired graft tolerance	[22–25]
Maladaptive coping / low resilience	Reduced vagal tone, ↑ sympathetic output	Exaggerated inflammatory responses; fatigue, poor recovery	[12,26–28]
Social isolation	↓ Oxytocin, ↓ parasympathetic activity	Higher inflammatory markers; slower rehabilitation	[1,8,28,29]
Effective psychological intervention (CBT, MBSR)	Normalised cortisol rhythm; reduced IL-6, CRP	Improved immune recovery; better graft adaptation	[23–25]

Abbreviations: HPA = hypothalamic–pituitary–adrenal; SAM = sympathetic–adrenal–medullary; CBT = cognitive-behavioural therapy; MBSR = mindfulness-based stress reduction; NK = natural-killer.

3.2. Cancer-related transplantation: Dual burden of stress and inflammation

Cancer-related transplantation creates a distinctive biobehavioural environment in which oncologic inflammation and surgery-induced immune perturbation coexist. Patients with a history of malignancy, such as renal-cell carcinoma survivors requiring kidney grafts, often exhibit residual inflammatory activation, circulating IL-6 and CRP elevations, and heightened vigilance toward bodily sensations [1,30]. The psychological residue of cancer-fear of recurrence, intrusive memories of treatment, and uncertainty about prognosis-interacts with the physiological demands of transplantation. These stressors amplify inflammatory signalling and compromise immune tolerance, increasing the likelihood of delayed graft function or secondary complications.

Longitudinal data in renal-transplant recipients indicate that depressive symptoms independently predict higher CRP and IL-6 levels up to 12 months after surgery, even when controlling for donor characteristics and immunosuppressant dosage [24]. Fatigue and sleep disturbance, two hallmark manifestations of systemic inflammation, correlate with both cytokine elevations and diminished health-related quality of life [21]. Such bidirectional feedback loops suggest that psychoneuroimmune dysregulation may sustain a chronic “inflammatory phenotype” long after surgical healing.

The dual burden also extends to behavioural and social dimensions. Cancer survivors often approach transplantation with a heightened sense of vulnerability, perceiving the procedure simultaneously as salvation and as renewed threat. This ambivalence can complicate adherence, increase healthcare utilisation, and strain caregiver relationships. Distress-related behaviours—poor appetite, disrupted sleep, and medication neglect—exacerbate metabolic stress and impair graft recovery. Conversely, patients who report meaning-making, spiritual coping, or strong social support display lower inflammatory markers and faster post-operative recovery. These findings collectively reinforce the notion that psychosocial context operates as an independent determinant of physiological adaptation.

Furthermore, residual effects of chemotherapy or radiotherapy may interact with stress pathways. Cytotoxic agents can induce mitochondrial dysfunction and oxidative damage that sensitise immune cells to catecholamine exposure, magnifying the inflammatory response during subsequent stress. Thus, cancer-related transplantation represents not only the convergence of two diseases but also of two stress biologies—oncologic and surgical—that continuously influence each other through immune and endocrine crosstalk. The psychoneuroimmunology framework therefore provides an essential lens for understanding why some recipients thrive while others experience protracted recovery despite equivalent surgical success.

3.3. Psychosocial screening and integrative rehabilitation

Given this mechanistic evidence, comprehensive psychosocial screening should form a routine component of transplant programmes that include cancer survivors. The hospital anxiety and depression scale (HADS) and the Distress Thermometer are well-validated instruments for identifying subclinical distress in both oncology and transplantation contexts [30,31]. Systematic screening allows clinicians to detect emerging psychological risks and initiate early, evidence-based interventions. Cognitive-behavioural therapy, mindfulness-based stress reduction, and resilience training have demonstrated efficacy not only for improving mood but also for modulating inflammatory biomarkers [22–24]. Integrating such interventions into standard transplant follow-up could thus influence both emotional well-being and immunological stability.

Implementation requires interdisciplinary coordination. Psychologists, transplant physicians, nurses, and rehabilitation specialists must collaborate to design integrative care pathways that link mental-health data with physiological indicators. Regular review meetings that include both medical and psychological teams can ensure that

treatment plans are adjusted dynamically in response to distress levels, adherence patterns, and biomarker changes [32].

Digital health tools and machine-learning analytics increasingly facilitate this integration by combining clinical, inflammatory, and behavioural datasets into predictive models [22,33]. These multimodal frameworks enable early identification of high-risk individuals and support personalised psycho-oncological rehabilitation strategies. For instance, algorithms can flag rising IL-6 or CRP levels in conjunction with elevated self-reported stress, prompting timely clinical review. Beyond prediction, digital monitoring fosters patient engagement by providing feedback on progress, empowering recipients to view psychological self-care as part of their medical treatment.

Finally, embedding psychoneuroimmunology education within transplant teams may shift institutional culture. Recognising that psychological care contributes directly to biological outcomes reframes mental-health support from optional to essential. Such a paradigm aligns with holistic oncology and precision medicine, ensuring that each patient's recovery plan addresses both molecular and emotional determinants of health. The ultimate goal is to transform cancer-related transplantation from a purely surgical intervention into a fully integrative process of biopsychosocial rehabilitation.

4. Clinical implications and integrative care strategies

4.1. Integrating psychosocial and biological assessment

Cancer-related organ-transplant recipients live under dual physiological and psychological stressors, combining the residual inflammation of malignancy with the biological demands of graft adaptation. Integrating psychosocial evaluation into transplant medicine is therefore not a complementary luxury but a clinical necessity [34]. Routine screening using validated instruments such as the hospital anxiety and depression scale (HADS) and the Distress Thermometer allows early detection of subclinical distress that might otherwise manifest through physiological deterioration or poor adherence [26,31,35].

In many transplant programs, pre-transplant psychological assessment has been linked with improved post-operative adherence, reduced hospital readmissions, and lower rates of acute rejection [27,36]. The value of these assessments lies not only in identifying overt psychopathology but in revealing subtle cognitive and emotional patterns that influence recovery behaviour. Patients with heightened threat vigilance or low perceived control often demonstrate poorer engagement with rehabilitation and medication routines. Recognising these traits early permits anticipatory counselling and behavioural planning before surgery.

A biopsychosocial approach requires that psychological and biological markers be monitored concurrently, forming a dynamic feedback system between emotional and physiological states. Routine measurement of cortisol rhythms, inflammatory cytokines such as IL-6, TNF- α , and CRP, and patient-reported stress levels enables timely intervention before irreversible immunological shifts occur [20]. Longitudinal monitoring of these markers can also help clinicians distinguish between biologically

driven inflammation and stress-related immune activation, which may appear similar in laboratory tests but respond to different treatments.

Digital health platforms have expanded the feasibility of such integrated monitoring [37]. Wearable devices and smartphone-based ecological momentary assessment can track sleep, heart-rate variability, and subjective mood in real time, providing early warning signals of psychological strain. Machine-learning algorithms can process these data streams to generate individualised risk profiles that alert clinicians when psychosocial stress reaches thresholds likely to influence immune stability. Embedding these tools within transplant follow-up not only improves responsiveness but empowers patients by visualising the tangible impact of stress management on physiological indicators.

Table 2 summarises the key screening instruments and psychological interventions commonly applied in psycho-oncological and transplant settings. These tools facilitate early detection of distress, structured treatment planning, and measurable improvements in immune–inflammatory regulation. Incorporating these approaches into clinical pathways enables personalised, biologically informed rehabilitation for cancer-related organ-transplant recipients.

Table 2. Screening instruments and psychological interventions in cancer-related transplantation

Tool/intervention	Primary target	Mechanistic or biological effect	Clinical evidence (Ref No.)
Hospital anxiety and depression scale (HADS)	Screening for anxiety and depressive symptoms pre- and post-transplant	Early identification of distress correlated with elevated IL-6 and CRP	[30–32]
Distress thermometer	Rapid quantification of global distress in oncology and transplant settings	Enables timely referral for psychosocial intervention before immune activation occurs	[30–32]
Mindfulness-based stress reduction (MBSR)	Emotional regulation, attentional control	Normalised diurnal cortisol rhythm, reduced sympathetic tone	[22–25,32,38]
Resilience or psycho-education training	Low coping resources, existential anxiety	Restored autonomic balance, improved HRV and immune recovery	[39,40]
Cognitive-behavioural therapy (CBT)	Maladaptive thoughts, low adherence, stress appraisal	↓ IL-6, ↓ CRP, improved T-cell proliferation and cytokine balance	[22–25,41,42]
Adherence therapy (CBT-informed)	Medication non-adherence in transplant patients	Enhanced self-efficacy and immunosuppressant compliance, reduced inflammatory load	[41,42]
Integrated psycho-oncology programme	Cross-disciplinary coordination within transplant care	Combined behavioural and biological monitoring for early intervention	[30,31,34,35,43,44]

Abbreviations: HADS = hospital anxiety and depression scale; CBT = cognitive-behavioural therapy; MBSR = mindfulness-based stress reduction; HRV = heart-rate variability.

4.2. Evidence-based psychological interventions

Psychological distress is a modifiable determinant of inflammatory tone, and targeted interventions can improve both emotional and physiological outcomes. Cognitive-behavioural therapy (CBT) and mindfulness-based stress reduction (MBSR) consistently demonstrate reductions in IL-6 and CRP, restoration of diurnal cortisol rhythms, and enhancement of immune recovery following surgery or chemotherapy [22,23,32,38]. Randomised controlled trials in cancer survivors have shown that resilience training, relaxation therapy, and psycho-education programmes significantly lower anxiety and depressive symptoms while improving sleep and functional well-being [39,40].

In transplant populations, CBT-informed adherence therapy has yielded substantial improvements in medication compliance and quality of life, indirectly

supporting graft stability and survival [41,42]. These effects arise partly through behavioural modification-better scheduling, problem-solving, and coping skill-but also through biological mechanisms involving reduced sympathetic tone and lower systemic inflammation. Evidence now supports the interpretation that psychosocial interventions are biologically active components of care rather than adjunctive comfort measures.

Furthermore, group-based interventions provide unique immunological advantages by fostering social connectedness and reducing isolation, a well-known amplifier of inflammatory signalling. Support groups, peer mentoring, and family-inclusive sessions build interpersonal trust and encourage collective coping strategies that buffer against physiological stress responses. Positive social interaction increases oxytocin and vagal activity, both of which possess anti-inflammatory properties. Integrating these relational dimensions into formal rehabilitation magnifies the biological impact of individual therapy.

For clinicians, delivering evidence-based interventions requires structured pathways and adequate training. Psycho-oncology specialists should collaborate with transplant teams to adapt existing oncology protocols-such as stress-management training or mindfulness curricula-to the specific context of organ transplantation. Incorporating these sessions into standard inpatient or outpatient follow-up reduces attrition and normalises mental-health support as part of medical care. Evaluating intervention efficacy should include both psychological metrics and biological markers, such as cytokine assays and immune-cell phenotyping, to capture the full spectrum of therapeutic benefit.

4.3. Toward precision psycho-oncology in transplantation

Advances in computational medicine now make it feasible to merge psychosocial and biomedical data within predictive frameworks that guide personalised care. Machine-learning-assisted risk stratification has already achieved accuracy comparable to conventional regression models in forecasting delayed graft function [32]. This success suggests a broader potential for psycho-immunologic analytics that integrate behavioural, hormonal, and immunological variables. By mapping the multidimensional trajectories of recovery, such systems could identify distinct subgroups of patients-those whose inflammation is primarily biologically driven versus those in whom psychological stress is the predominant trigger.

Multimodal datasets can inform the timing, intensity, and type of psychosocial intervention required [45]. For instance, patients displaying both elevated IL-6 and high self-reported distress may benefit from early initiation of structured stress-management programmes, while those with stable biomarkers but poor coping might prioritise behavioural coaching and peer support. Over time, these precision frameworks could evolve into adaptive clinical decision tools that personalise both immunosuppressant dosing and psychological therapy schedules based on integrated biological feedback.

Interdisciplinary collaboration is fundamental to achieving this precision model. Psycho-oncology teams should include psychiatrists, clinical psychologists, transplant physicians, nurses, social workers, and data scientists working in synchrony.

Multidisciplinary case reviews enable comprehensive interpretation of patient progress, linking molecular data with lived experience. Such integrated teams have been associated with improved adherence, reduced rehospitalisation, and higher long-term survival across complex oncologic populations [44,45].

Ethical and educational considerations accompany this integration. Clinicians must ensure data privacy, informed consent, and transparent communication regarding algorithmic predictions. Equally important is fostering digital literacy among patients so that they understand how psychological input contributes to their biological recovery. Educational initiatives that explain psychoneuroimmunology principles can empower patients to participate actively in self-regulation, viewing mental-health care as a vital component of survival rather than an optional adjunct.

Finally, embedding psychological support across the entire transplant continuum—from evaluation and surgery to long-term surveillance—represents a transformative step in clinical practice. Routine psychosocial assessment, continuous biomarker tracking, and tailored interventions together create a closed-loop system for holistic recovery. The integration of psychological science with immunology and computational analytics moves psycho-oncology toward a genuinely precision-oriented discipline. In this model, each patient’s emotional landscape is treated as a measurable, modifiable, and biologically meaningful factor in transplant success. Such an approach realises the ultimate goal of psycho-oncological medicine: uniting mind and body within a single continuum of healing.

The overall architecture of this multimodal integration is summarised in **Figure 2**, which illustrates how donor, perfusion, and psychosocial data can be synchronised through AI-assisted predictive analytics to generate personalised intervention plans and adaptive biological feedback within cancer-related transplantation.

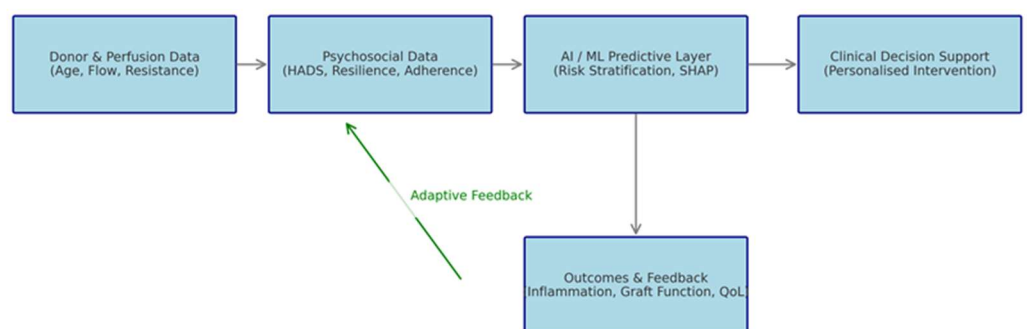


Figure 2. Multimodal integrative framework linking donor, perfusion, and psychosocial data through AI-assisted prediction to inform personalised clinical interventions and adaptive feedback for cancer-related organ transplantation.

5. Conclusion

Cancer-related organ transplantation represents one of the most complex clinical frontiers where biological recovery and psychological adaptation must proceed in

parallel. The evidence reviewed throughout this paper demonstrates that mind and body are not separate dimensions of the healing process but mutually regulating systems. Emotional distress, when prolonged or unaddressed, can trigger neuroendocrine activation, sustain inflammatory signalling, and impair graft adaptation. Conversely, psychological stability, social connectedness, and purposeful coping can enhance immune tolerance and support tissue regeneration. These bidirectional relationships confirm that psychological care is not a peripheral service but a determinant of clinical outcome.

From a mechanistic standpoint, the psychoneuroimmunology framework provides a scientific rationale for integrating psychological assessment into every stage of transplant care. The hormonal and cytokine networks that mediate stress responses are the same pathways influencing rejection, infection, and recovery. Recognising this overlap shifts the traditional focus of transplantation from a purely surgical or pharmacological procedure toward a holistic model of systemic regulation. By monitoring stress-related biomarkers alongside standard immunologic indicators, clinicians can intervene before molecular imbalance evolves into overt pathology.

Clinically, these insights translate into a new mandate for interdisciplinary collaboration. Surgeons, oncologists, psychiatrists, psychologists, nurses, and rehabilitation specialists must function as a unified team. Routine psychosocial screening, personalised counselling, and structured interventions such as cognitive-behavioural therapy or mindfulness training should be implemented with the same priority as immunosuppressant management. When psychological support is embedded as standard care, improvements occur not only in emotional well-being but also in adherence, inflammation control, and overall survival.

Technological progress further expands what integrative medicine can achieve. Digital monitoring, wearable biosensors, and machine-learning analytics now enable continuous tracking of emotional and physiological data. These tools can alert clinicians to rising stress or inflammation and prompt timely intervention, effectively transforming psycho-oncological care into a real-time preventive system. However, ethical oversight remains essential. Protecting patient privacy, ensuring informed consent, and maintaining transparency in algorithmic recommendations are prerequisites for responsible innovation.

The ultimate implication of this synthesis is conceptual as much as practical. Viewing the transplant recipient as a biopsychosocial organism rather than a surgical subject redefines what constitutes successful recovery. Psychological resilience, emotional regulation, and interpersonal trust become measurable components of medical prognosis. Such an approach aligns with the broader evolution of precision medicine, where biological and behavioural data converge to guide truly personalised care.

In summary, integrating psychoneuroimmunology into cancer-related transplantation transforms a complex clinical challenge into an opportunity for holistic healing. The convergence of oncology, immunology, and psychological science marks a paradigm shift: recovery is no longer measured solely by graft survival but by the restoration of systemic harmony between mind and body. Sustaining this harmony demands continuous collaboration, compassionate communication, and scientific vigilance. As psycho-oncology advances toward precision and integration, its central

message remains profoundly human—the mind is an active participant in the biology of survival.

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