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Stress predicts the trajectory of wound healing in living kidney donors as measured by high-resolution ultrasound



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ARTICLE INFO

Article history: Received 28 March 2014 Received in revised form 6 June 2014 Accepted 15 June 2014 Available online 25 June 2014

Keywords: Stress Personality Wound healing Kidney donor Transplant Transplantation

ABSTRACT

Background: Psychological stress has been shown to be an influential factor on the rate of wound healing; however these findings have been demonstrated predominantly on artificially created wounds. Due to the absence of major co-morbidities, living kidney donors are a unique group in which to study this relationship. This study investigated the effect of preoperative stress and personality on surgical wound healing through the use of high-resolution ultrasound.

Methods: Living kidney donors due to undergo a hand-assisted laparoscopic donor nephrectomy were asked to complete the Perceived Stress Scale, the Life Orientation Test-Revised and the Ten Item Personality Inventory prior to surgery. High-resolution ultrasound scans of surgical wounds were performed on the first three post-operative days and once following discharge (mean = 15.3 days; s.d. 2.8). Two measurements from each image were obtained: wound width (size of wound) and median intensity (a marker of tissue fluid). Latent Growth Curve Models (LGCMs) were used to evaluate wound healing. Results: 52 living kidney donors participated. Higher pre-operative life stress, lower optimism and lower conscientiousness were associated with delayed wound healing in living kidney donors for both outcomes. Increased emotional stability was associated with faster wound healing as demonstrated by a change in median intensity. Possible confounding factors, such as age, BMI, smoking status, local anaesthetic use and wound drain placement were not influential.

Conclusions: This study, which measured wound healing in a novel patient sample using a novel technique, has demonstrated a negative association between stress and wound healing and the positive influence of optimism, conscientiousness and emotional stability.

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1. Introduction

Psychological stress has been shown to be an influential factor on the rate of wound healing in different parts of the body, in different clinical circumstances and through the use of different

Abbreviations: AIC, Akaike information criteria; BIC, Bayesian information criteria; BMI, Body Mass Index; CFI, Comparative Fit Index; CRP, C-reactive protein; eGFR, estimated Glomerular Filtration Rate; LGCM, Latent Growth Curve Model; LOT, Life Orientation Test; LOT-R, Life Orientation Test-Revised; MI, median intensity; MLR, Maximum Likelihood estimator; RMSEA, Root Mean Square Error of the Approximation; TLI, Tucker Lewis Index; WW, wound width.

modalities (Gouin and Kiecolt-Glaser, 2011). A wound is defined as a disruption of normal anatomical structure and function (Lazarus et al., 1994) and healing of any wound necessitates a step-wise process in which a variety of different inflammatory mediators are involved to facilitate repair to the damaged area. The wound healing process is dependent on a broad range of internal and external factors, one of which is a fully functional immune system that is able to respond appropriately to tissue injury (Walburn et al., 2009). It is through the immunological pathway that stress is thought to have a modulatory influence (Segerstrom and Miller, 2004) via activation of the hypothalamicpituitary-adrenal axis and the sympathetic-adrenal-medullary axis. It is also recognised that stress can have significant behavioural effects, for example on diet (Torres and Nowson, 2007) and sleep (Ohayon, 2009), which, in turn, affect the speed of wound healing.

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Although the link between psychological stress and healing is well established, there are few studies that have evaluated cutaneous surgical wounds (Holden-Lund, 1988; Scheier et al., 1999; Broadbent et al., 2003, 2012; Doering et al., 2005). These studies have demonstrated that increased psychological stress is associated with an increase in wound complications, such as infection (Doering et al., 2005; Scheier et al., 1999), and reduced levels of inflammatory markers, such as interleukin-1 (IL-1) and metalloproteinase-9 (MMP-9) (Broadbent et al., 2003). Randomised studies of psychological intervention to minimise stress in surgical patients have demonstrated an improvement in wound healing in the intervention group (Holden-Lund, 1988; Broadbent et al., 2012).

Living kidney donors are a unique group of patients in which to examine the association between stress and surgical wound healing for two reasons. Firstly, they are patients who, prior to surgery, are extensively screened for both physical and psychological pathologies and are only allowed to donate if fit. They should therefore be free from all major physical and psychological comorbidities that may directly affect wound healing. Secondly, they are healthy but undergo major surgery for the benefit of another individual, with no physical benefits to themselves. It is therefore crucial that they recover quickly from the procedure with few complications in order to minimise the physical trauma of surgery. The risk of death from living kidney donation is currently quoted as 3 in 10,000 donations (Segev et al., 2010) and the rate of any morbidity (defined as "the incidence of at least any one complication per donor") is 10.3% for laparoscopic living donor nephrectomy and 15.7% for open surgery (Hadjianastassiou et al., 2007). The rate of wound infection for donors undergoing hand-assisted laparoscopic donor nephrectomy is 2.2% (Matas et al., 2003, Pareek et al., 2006).

The evaluation of potential living kidney donors is carried out according to an evidence-based protocol which involves a series of appointments and investigations. A full assessment is undertaken by a nephrologist and a transplant surgeon who elicit a detailed medical and surgical history from the donor. The aim of this is to determine whether there are any potential contraindications to donation. A detailed physical examination is performed to assess for potentially undiagnosed pathologies and also to permit planning for surgery. A number of medical tests are routinely performed including urinalysis, blood tests, virology and infection screens, cardiac investigations (i.e. electrocardiography) and radiological examinations, such as a chest X-ray. A detailed assessment of kidney function is also performed and includes radiological tests, such as an ultrasound and either a computerised tomography scan (CT scan) or an angiogram.

Guidelines regarding the psychological assessment of living donors are less prescribed and a formal evaluation of the donor's psychological state is not mandated. Referral to psychological services is recommended when requested by the patient or when an issue is detected as part of the workup process. The relative psychological contraindications to living kidney donation are previous or current mental health illness, active substance abuse, dependence on prescribed medication, self-harming behaviour or significantly dysfunctional family relationships, particularly between recipient and donor. Over a thousand living donor procedures take place across the UK each year (NHS Blood and Transplant, 2013). The process of donating a kidney is often very stressful for a donor, not just because of their own operation but because a loved one is frequently undergoing an operation on the same day. To date, no evaluation has been made as to whether there are any modifiable factors that may predict recovery from surgery in these patients.

In addition to stress, personality has also been shown to impact upon health outcomes, both directly through physiological

mechanisms and indirectly through patient behaviour. Conscientiousness is thought to lead to a healthier, longer life through the collective reduction of many small risks, which result from conscientious behaviour. Further, highly conscientious individuals report fewer daily stresses (O'Connor et al., 2009) and engage in more adaptive coping styles (Grant and Langan-Fox, 2006; Kern and Friedman, 2008), suggesting that personality may moderate the potentially damaging effects of stress, which has been referred to as the stress moderation model (Weibe et al., 2010). Lower levels of optimism have been associated with slower wound healing (Ebrecht et al., 2004) and an increase in wound infection and allcause rehospitalisation after coronary artery bypass graft surgery (Scheier et al., 1999). Combinations of personality traits have also been demonstrated as being particularly harmful, such as a low level of conscientiousness coupled with high neuroticism, which leaves an individual at high risk of poor health outcomes (Friedman and Kern, 2014).

The aim of this study was to evaluate the trajectory of wound healing in living kidney donors using high-resolution ultrasound, and to ascertain what potentially modifiable factors predict recovery. High resolution ultrasound (HRUS) was the chosen modality to assess wound healing because it provides an objective, reliable, non-invasive method of quantitatively assessing structural changes deep within a wound that correlates highly with tissue histology, photography and nuclear magnetic resonance spectroscopy (Dyson et al., 2003; Harland et al., 1993; Hu et al., 1998; Rippon et al., 1998). The HRUS machine provides a detailed image of the different layers of the skin, through which the size of the wound and differences in the fluid content can be measured. HRUS has been used on one previous occasion to investigate the association between wound healing and stress (Ebrecht et al., 2004) and although the use of HRUS to measure skin tissue fluid content has not previously been used in psychological research, it has been extensively validated in other studies (Gniadecka et al., 1994, 1995; Seidenari and Di Nardo, 1992a,b).

Specifically we tested the following hypothesis: pre-operative life stress will predict the trajectory of wound healing. Given the prediction of the stress-moderation model, we also explored whether optimism and the 'Big Five' personality factors were predictive of wound healing, and tested if interactions between stress and personality predicted the rate of wound healing.

2. Materials and methods

2.1. Design

This study was conducted between August 2012 and May 2013 and used a prospective observational design. Patients completed questionnaires between 1 and 2 weeks preoperatively. Wounds were evaluated during hospital admission (days 1, 2 and 3) and at follow up, approximately 2–3 weeks after surgery.

2.2. Sample

A consecutive sample of living kidney donors from a single centre donating over a six month period were recruited (n = 58). The sample included adult donors principally from the south east of England but also from across the United Kingdom (UK) and overseas. Exclusion criteria included anyone who was unable to speak or read English without the use of an interpreter. Donors were approached by a researcher on one occasion two to four weeks prior to scheduled surgery, following completion of all medical tests and appointments. Formal written consent was obtained. NHS research ethics approval for the study was obtained (09-H0804-31).

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