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MINIREVIEWS

Post-transplant erythrocytosis after kidney transplantation: A review

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Abstract

Post-transplant erythrocytosis (PTE) is defined as persistently elevated hemoglobin > 17 g/dL or hematocrit levels > 51% following kidney transplantation, independent of duration. It is a relatively common complication within 8 months to 24 months post-transplantation, occurring in 8%-15% of kidney transplant recipients. Established PTE risk factors include male gender, normal hemoglobin/hematocrit pre-transplant (suggestive of robust native kidney erythropoietin production), renal artery stenosis, patients with a well-functioning graft, and dialysis before transplantation. Many factors play a role in the development of PTE, however, underlying endogenous erythropoietin secretion pre-and post-transplant is significant. Other contributory factors include the renin-angiotensin- aldosterone system, insulin-like growth factors, endogenous androgens, and local renal hypoxia. Most patients with PTE experience mild symptoms like malaise, headache, fatigue, and dizziness. While prior investigations showed an increased risk of thromboembolic events, more recent evidence tells a different story-that PTE perhaps has lessened risk of thromboembolic events or negative graft outcomes than previously thought. In the evaluation of PTE, it is important to exclude other causes of erythrocytosis including malignancy before treatment. Angiotensin converting enzyme inhibitors (ACE-I) and angiotensin receptor blockers (ARBs) are the mainstays of treatment. Increased ACE-I/ARB use has likely contributed to the falling incidence of erythrocytosis. In this review article, we summarize the current literature in the field of post-transplant erythrocytosis after kidney transplantation.

Key Words: Post-transplant erythrocytosis; Kidney transplantation; Epidemiology; Treatment; Guidelines; Outcomes

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Core Tip: Post-transplant erythrocytosis is an important disease process after kidney transplantation that manifests in a typical population based on risk factors, responds well to pharmacotherapy in most cases, and over time, has led to minor sequelae and favorable outcomes with minimal impact on patient and allograft survival. It is important to recognize this disease for appropriate management as well as investigation for other more ominous causes of erythrocytosis, namely malignancy.

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INTRODUCTION

Although renal transplantation remains the treatment of choice for patients with end-stage renal disease, many patients develop post-transplant complications that require close follow-up and proper management[1,2]. Post-transplant erythrocytosis (PTE), one such complication, is commonly defined as persistently elevated hemoglobin (Hgb) > 17 g/dL or hematocrit (Hct) > 51% following kidney transplantation[3]. The purpose of this review article is to outline the current knowledge of epidemiology, clinical manifestations, risk factors, pathogenesis, clinical management, and outcomes of PTE. This schema is illustrated in flowchart form in Figure 1.

METHODS

We conducted literature searches in PubMed, EMBASE, Cochrane, CINAHL (Cumulative Index to Nursing and Allied Health Literature) from database inception to February 2021, as well as Google Scholar and reference lists of relevant studies and reviews. We limited our search to studies with available full text and English language.

EPIDEMIOLOGY

PTE was first described in a case report from 1965 of a 22-year-old woman undergoing kidney transplantation with bilateral nephrectomy and splenectomy[4]. The incidence of PTE, as described in the literature, ranges from 8%-15%, with some studies as low as 2.2% and as high as 22.2%[3,5,6]. This variability can be explained partly by three main factors: (1) Lack of consensus regarding the definition of PTE; (2) The increase in use of angiotensin-converting enzyme inhibitors (ACE-I), angiotensin receptor blockers (ARBs); and (3) Aggressive use of potent immunosuppressive agents, including mycophenolic acid (MPA) derivatives.

The ambiguity surrounding the definition of PTE has made it difficult to evaluate disease prevalence and risk factors. For example, differing reference limits for Hgb based on biological sex pose a major challenge to defining PTE. As is described in the literature, Hgb/Hct levels vary between men and women based primarily on androgen levels among other factors. Some studies have reported gender-specific cutoffs (53%-55% for men and 48%-51% for women), others have used duration of increase, and others have just used the same threshold to define PTE in both women and men[1,7-10]. To establish consensus in the field in terms of diagnosis and management, the Kidney Disease Improving Global Outcomes (KDIGO) organization, in 2009, formed a workgroup where they defined PTE as Hgb > 17 g/dL or Hct > 51% independent of gender and duration[11]. While these are widely accepted guidelines, additional guidelines from both the United States and Europe have emerged over time [11-14]. These are summarized in Table 1.

The widespread use of ACE-I and ARBs has been linked with the declining incidence of PTE. ACE-I/ARBs became mainstays of PTE treatment after many clinical trials in the late 1990s to early 2000s showed high efficacy in reducing Hgb in kidney

Table 1 Post-transplant erythrocytosis management guidelines

Ref.	Society	Recommendations
KDIGO Transplant Work Group[11], 2009	KDIGO	Definition of erythrocytosis: hemoglobin > 17 g/dL or hematocrit > 51%. Recommend using ACE-Is or ARBs for initial treatment of erythrocytosis.
Bia *et al*[12], 2010	NKF/KDOQI	Recommend treatment when hemoglobin > 17-19 g/dL or hematocrit > 51%-52%. Treatment guidelines per 2009 KDIGO recommendations.
Baker *et al*[13], 2017	The Renal Association	Recommend treatment when hematocrit > 52% in males and > 49% in females. Recommended first line treatment is ACE-I or ARBs.
McMullin *et al*[14], 2019	British Society of Hematology	Treat if hematocrit is persistently elevated for > 1 mo with ACE-I or ARB. Therapeutic phlebotomy can be used for persistent symptoms, but there is no evidence of benefit. No evidence for aspirin as an effective treatment.

KDIGO: Kidney Disease Improving Global Outcomes; ACE-I: Angiotensin converting enzyme inhibitors; ARB: Angiotensin receptor blocker; NKF: National Kidney Foundation; KDOQI: Kidney Disease Outcomes Quality Initiative.

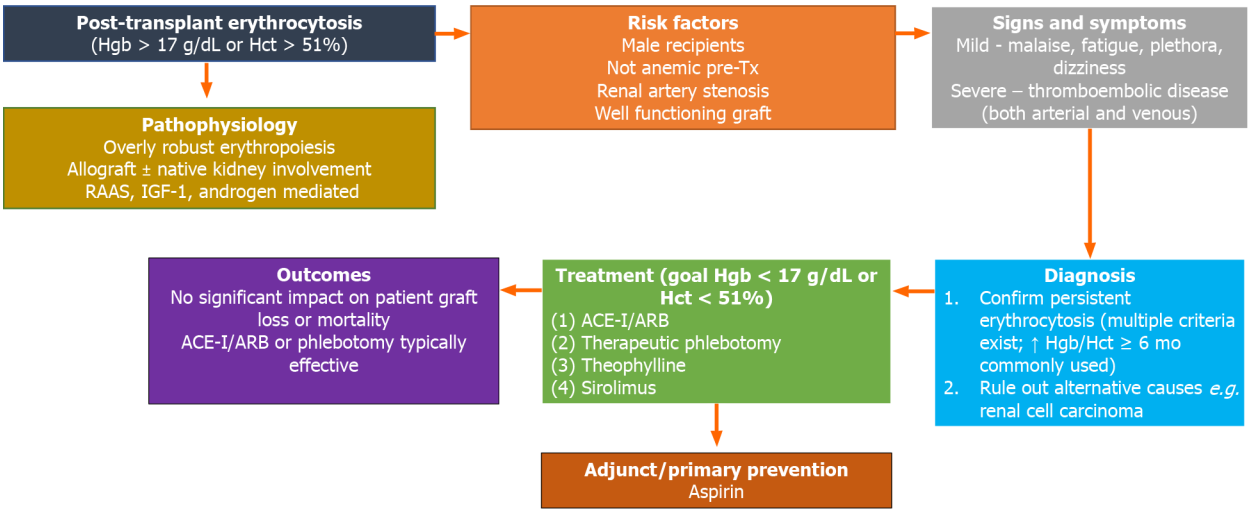

Figure 1 Post-transplant erythrocytosis. Post-transplant erythrocytosis (PTE) is a complication after transplant due to overly robust erythroid production from the allograft plus/minus native kidneys. Typically, the disease is mild as it is recognized early with laboratory screening. Accurate diagnosis is key to not miss renal cell carcinoma. Angiotensin converting enzyme inhibitors/angiotensin receptor blocker or phlebotomy are commonly effective treatments. Aspirin is often used for primary prevention though no studies to date support its use. PTE is not associated with graft loss or patient mortality. Hgb: Hemoglobin; Hct: Hematocrit; RAAS: Renin-angiotensin-aldosterone system; IGF: Insulin growth factor; Tx: Transplant; ACE-I: Angiotensin converting enzyme inhibitors; ARB: Angiotensin receptor blocker.

transplant recipients (KTRs)[15-38]. These are illustrated in Table 2, which was based on the previous work of Vlahakos *et al*[3] with the addition of pertinent studies upon our review[3,25-38]. These will be further elaborated on in our subsequent section on treatment.

In a study examining this hypothesis between erythrocytosis and renin-angiotensin-aldosterone system (RAAS) blockade the incidence of erythrocytosis (defined Hct > 51%) had fallen from 19% of those transplanted between 1993-1996 to 8% of those between 1997-2005 - a fall of more than 50% with greater use of ACE-I/ARBs[5]. Not many studies have investigated the relation of induction agents to the incidence of PTE. In a study of 131 KTRs examining lymphocyte depleting induction and PTE incidence, an association was observed, but this was not statistically significant (P = 0.375)[5].

In short, PTE occurs in around 10%-15% of KTRs and has likely decreased both in incidence and prevalence over time with increased utilization of ACE-I/ARBs playing a significant role.

RISK FACTORS

Well-established risk factors for PTE have been described over the past few decades.

Table 2 Effect on hemoglobin and hematocrit after use of angiotensin converting enzyme inhibitor/angiotensin receptor blocker

Ref.	Number of patients	Hgb pre (g/dL)	Hgb post (g/dL)	*P* value	Hct pre (%)	Hct post (%)	*P* value	Drug (mg/d)	Duration (wk)
Islam *et al*[15], 1990	7				56	45	< 0.001	Captopril 75	NA
Conlon *et al*[16], 1993	11				52	46	< 0.05	Enalapril 2.5	12
Rell *et al*[17], 1994	17				51	43	< 0.01	Enalapril 20	12
Wong *et al*[18], 1994	14				53	44	< 0.0001	Enalapril 2.5-5	
Torregrosa *et al*[19], 1994	19				56	47	< 0.001	Captopril 25	12
Danovitch *et al*[20], 1995	15				53	46	< 0.001	Enalapril 5	8
Hernández *et al*[21], 1995	21				58	49	< 0.01	Captopril NA	24
Mulhern *et al*[22], 1995	8				54	43	< 0.05	Enalapril 8.5	12
Perazella *et al* [23], 1995	10				52	44	= 0.001	Enalapril 3.5	24
Rostaing *et al* [24], 1995	12				51	42	< 0.001	Enalapril 14	6
Ok *et al*[25], 1995	10				57	45		Enalapril 10	8
Conlon *et al*[26], 1996	7				55	49	0.001	Losartan 50	12
Morrone *et al*[27], 1997	20				52	48	< 0.05	Enalapril 10	NA
Ducloux *et al*[28], 1998	4				52	38	< 0.0005	Losartan 100	12
Mazzali and Filho [29], 1998	27				56	46	< 0.05	Enalapril 5	12
Julian *et al*[30], 1998	23				53	49	< 0.01	Losartan	8
Montanaro *et al*[31], 2000	11				54	46	< 0.01	NA	NA
Glicklich *et al*[32], 2001	10				53	45	< 0.01	Lisinopril or fosinopril	6.8
Trivedi *et al*[33], 2003	9	17.2 ± 0.6	14.9 ± 1.4	0.0023	51.3 ± 2.4	43.7 ± 4.6	0.003	Fosinopril, 10-20	12
Stoll *et al*[34], 2004	1	20.7	18.2	NA	58	53	NA	Losartan, 25-50	8
Esposito *et al*[35], 2007	27	16.5	15	< 0.0001	52	45.2	< 0.0001	Ramipril, 1.5-10	52
Bravo *et al*[36], 2008	6	15.9	14.5 ± 0.7	0.001				Lisinopril 1.5-5	52
Ahmed *et al*[37], 2012	12	16.79 ± 0.75	15.17 ± 1.72	NA	54.78 ± 1.96	48.61 ± 1.85	NA	Enalapril	NA
Almonte *et al*[38], 2015	1	17.5	15	NA	53	44.5	NA	Enalapril 0.13 mg/kg/d	24

Hgb: Hemoglobin; Hct: Hematocrit; NA: Not available.

These known risk factors include the male gender[3,38-41], retention of a native kidney with adequate erythropoiesis before transplant[3,5,37,38,40,42-45], renal artery stenosis [38,39,46] and patients with a well-functioning graft[3,37,40,44,47]. These risk factors are consistently present in the majority of recipients who develop PTE.

Age and pre-transplant dialysis need may also contribute to PTE as demonstrated in the following studies. In their study published in 2021, Alasfar *et al*[6] noted younger recipient, young donor age and polycystic kidney disease were risk factors associated with the development of PTE. In our own examination of PTE in KTRs at our institution, we found that non-preemptive transplant was significantly associated with

the development of PTE [hazard ratio (HR) =2.32 (95%CI (confidence interval): 1.55-3.47), $P < 0.001$, on univariate analysis); HR = 3.86 (95%CI: 1.56-9.56) $P = 0.003$ on multivariate analysis)][41]. These recently-published risk factors are highly plausible, but more studies will need to corroborate them before we consider them well-established risk factors.

The evidence linking PTE to certain immunosuppressive agents is mixed. In one study that examined the incidence of PTE with the maintenance immunosuppressive regimen, MPA was significant in reducing the incidence of PTE ($P = 0.002$) while neither sirolimus ($P = 0.315$) or azathioprine ($P = 0.6915$) were significant[5]. In another study, patients treated with sirolimus had a lower incidence of PTE than those treated with mycophenolate mofetil (7% *vs* 19% respectively; $P = 0.013$)[48]. In addition, sirolimus was found to be negatively correlated with PTE [odds ratio = with sirolimus = 0.33, (95%CI: 0.12 to 0.89), $P = 0.028$]. Similarly, another study showed no differences in Hct or erythropoietin levels among the renal transplant population who were chronically treated with prednisone and azathioprine, prednisone and cyclosporine, or prednisone, azathioprine, and cyclosporine[49]. These findings are interesting, particularly those pertaining to mycophenolate and azathioprine as in theory, all antiproliferative agents ought to incur bone marrow suppression, reduce erythropoiesis or PTE, and subsequently lead to post-transplant anemia. The mechanisms of these discrepancies are unclear and could contribute to variable incidence levels.

There is also evidence that factors, in addition to erythropoietin, may increase the risk of PTE. As we have implied and will describe in further sections, the RAAS plays a key role in the development of PTE. Endogenous androgens and insulin-like growth factor 1 (IGF-1) have also been implicated[3]. Androgens may increase the response of erythroid precursors to erythropoietin[27]. Other studies have reported increased serum levels of IGF-1 and IGF binding proteins in patients with PTE, suggesting that IGF-1 plays some role, either directly or indirectly, in the regulation of erythropoiesis. This was especially prevalent in patients that did not have increased erythropoietin production[27,50,51]. A decrease in renal blood flow, usually due to renal artery stenosis, leading to local renal hypoxia may also contribute[46]. How these relate to the development of PTE will be described in our section on pathophysiology.

In summary, well established risk factors predict the development of PTE. While many of these are unmodifiable, knowledge of them can help predict likelihood of disease and impact surveillance/management. For those that are modifiable, they offer opportunities for clinicians and researchers alike to evaluate therapeutic impact, gain understanding of the disease and improve outcomes.

PATHOPHYSIOLOGY

PTE generally develops in KTRs with well-functioning allografts, as demonstrated by lower serum creatinine at diagnosis compared to controls, as well as in patients with no evidence of acute or chronic rejection[3,37,40,47,52]. A successful graft begins to secrete erythropoietin within 3 days of transplant. As this secretion begins, the anemia that most patients have before transplant corrects between three months and one-year post-transplant[53]. In normal physiology, secretion of erythropoietin then decreases [53]. If erythropoietin secretion does not decrease, PTE develops[39]. It is unclear why erythropoietin continues to be secreted in these cases; however, because most KTRs with PTE still have their native kidneys, it is thought to be due to erythropoiesis driven by both the allograft and native kidneys[3,38,42,54]. Vlahakos *et al*[3] group describes this process akin to the uncoupling and loss of feedback that occurs in the parathyroid glands after prolonged secondary hyperparathyroidism, describing this autonomous unregulated erythropoietin secretion as "tertiary hypererythropoetinemia". The connection between PTE and serum erythropoietin levels, though, is not clear-cut. At the time of PTE diagnosis, many studies found no increase in serum erythropoietin for KTRs with PTE when compared to controls[39,50,55]. However, PTE was found to develop in KTRs who have adequate erythropoietin levels before transplant, while those with low levels of erythropoietin before transplant were less likely to develop PTE. Thus, pre-transplant human erythropoietin treatment to correct low levels may be "protective" against PTE by decreasing the sensitivity of erythroid precursors to erythropoietin[3,55].

As mentioned previously, erythropoietin production is derived from multiple redundant pathways involving the RAAS system, IGF-1, and endogenous androgens that in turn are implicated in PTE[3,27,50,51]. In terms of the RAAS system, as shown in both murine models and human subjects *via in vivo* administration as well as *via*

ACE-I/ARB use, renin and angiotensin II are linked with erythropoiesis[3,56]. IGF-1 and endogenous androgens similarly impact erythropoiesis directly as well as indirectly *via* the RAAS system as demonstrated by androgen-mediated renin production and studies showing ACE inhibition leads to decreased IGF-1 Levels[3,27,32,50]. N-acetyl-seryl-aspartyl-lysyl-proline (ac-SKDP) is an important inhibitor of erythropoiesis, which is augmented by ACE-I/ARB use *via* blocking ACE, which degrades ac-SKDP. Therefore, ACE-I/ARB use leads to decreased ac-SKDP[57].

While more research is needed to learn even more about PTE, novel discoveries of the often overlapping mechanisms causing PTE have improved our understanding of this disease and its management.

CLINICAL PRESENTATION

PTE often occurs anywhere between eight months and two years after kidney transplantation. Hgb and Hct levels gradually rise over a few months during this time period. The clinical manifestations of PTE range from quite mild (malaise, fatigue, plethora, lethargy, dizziness) to more severe thromboembolic events, though these are quite rare in modern times. Possible thromboembolic events documented include deep venous thrombosis (DVT), pulmonary embolism (PE), and ischemic stroke. About 1%-2% die of complications if not treated[58]. However, a recent study found no correlation between PTE and vascular thromboembolism or patient mortality due to early diagnosis and aggressive management[41]. In 25% of those who are not treated, PTE spontaneously resolves within two years of diagnosis. In the rest of untreated patients, PTE tends to persist for a few years and usually resolves as kidney function ergo erythropoietin production declines due to calcineurin inhibitor use, hypertension, post-transplant diabetes mellitus, acidosis, acute kidney injuries, and chronic rejection [58].

In essence, PTE is often discovered *via* routine laboratory monitoring that is standard to post-transplant care, leading to relatively mild, often self-limited disease due to decreasing allograft function over time.

DIAGNOSTIC EVALUATION

The diagnostic evaluation of PTE is a two-step process: confirmation of persistent erythrocytosis and exclusion of common causes of nontransplant-erythrocytosis[58]. Persistent erythrocytosis is defined as a Hgb > 17 g/dL and/or Hct > 51% that persists for more than six months post-transplant. However, all patients with elevated Hgb or Hct should first be evaluated for hemoconcentration (extracellular volume contraction) as a reason for erythrocytosis, though this would typically cause an acute elevation rather than chronic.

Once the persistence of elevated Hgb/Hct is established, a diagnostic workup needs to be done to exclude alternative causes of erythrocytosis. The workup is different in patients with possible PTE compared to those with erythrocytosis who have not received a transplant because a thorough evaluation is completed before transplant as part of the selection process. This pre-transplant evaluation confirms a baseline Hgb and Hct and usually excludes significant pulmonary disease and congenital disorders. Thus, further workup in post-transplant patients involves excluding malignancy (such as breast cancer, renal cell carcinoma, and hepatocellular carcinoma), renal artery stenosis, and obstructive sleep apnea. Erythropoietin concentrations are not commonly measured as part of evaluation because there has not been documented evidence of correlation between PTE and serum erythropoietin levels[58].

In brief, the diagnosis of PTE is made by confirming the presence of persistent erythrocytosis and then ruling out often indolent potential causes of erythrocytosis not uncovered *via* recipient evaluation.

TREATMENT

Given the potentially devastating complications of thromboembolic events associated with polycythemia, the KDIGO organization recommended treating PTE in their 2009 *Transplant Recipient* guidelines[11]. Consistent with treatment goals of other causes of polycythemia, the target Hct should be less than 51% or a Hgb less than 17.5[14,54].

While 20%-30% of patients may have long term resolution of their PTE, due to the large proportion of relapse, it is recommended that treatment, in most cases, continue indefinitely[3].

As previously mentioned, the foundation of PTE treatment is with either ACE-I or ARBs. RAAS inactivation has been documented to cause dose-dependent decrease in Hct levels, though the exact mechanism behind this decrease is not fully understood[3,39,42]. The most likely hypothesis proposed is that ACE-I impair red blood cell production to improve PTE[23]. As described previously, ACE-I/ARBs impact several pathways implicated in erythropoietin production including the RAAS system, endogenous androgens, and IGF-1[3,27,32,50,51,56]. Treatment with ACE-I or ARBs begin to take effect within one month with a nadir in Hct seen around three months. This level has shown to be sustained in long term studies up to 1-3 years[3].

In their study from 2001, Yildiz *et al*[59] conducted a direct comparison between an ACE-I (enalapril) to an ARB (losartan) showed that both effectively lowered the Hgb of PTE patients by > 1 g/dL. Enalapril did show a larger drop in Hgb than losartan (P = 0.05). Withdrawal of either agent did lead to relapse of PTE in most patients, however the time to relapse was longer in the losartan arm of the study (P = 0.11)[59]. Generally, both drug classes are well tolerated, with ARBs known to have fewer side effects than ACE-I. Both classes of medications are quite effective, with a reported refractory rate of 22% to ACE-I/ARBs. Patients with pre-transplant ACE-I/ARB use have shown to have higher rates of refractoriness, although an exact mechanism for this observation has not been validated[59].

As indicated in Table 2, based on the work of Vlahakos *et al*[3] with the addition of recent pertinent studies, relatively small doses of ACE-I or ARBs were able to significantly decrease Hgb/Hct levels by at least 1 g Hgb/3 points Hct and medically manage PTE.

In patients that either cannot tolerate ACE-I/ARBs, have contraindications to them, or do not have a treatment response, second line therapies include phlebotomy or theophylline[3]. Phlebotomy has long been effective in lowering Hct and Hgb values, with one study showing that it decreased Hct by approximately 10% within two weeks [60]. Patients who chose this route should be started on iron supplementation as serial phlebotomy can lead to severe iron deficiency[3]. For patients who prefer to avoid phlebotomy, theophylline is a potential option as a second line therapy, though results are mixed[25,33,61-63].

Theophylline, an adenosine antagonist, is believed to directly modulate the release and effect of erythropoietin by stimulation of the A2 receptor. Theophylline has had varied results in several studies. As described in 3 studies, theophylline has been shown to decrease Hct by 4%-15% in patients with PTE[61,62,64]. Notably, in the 2 studies cited whereby Hct after theophylline administration, one was case report (n = 1) who discontinued theophylline after four weeks due to side effects, while the other study (Trivedi *et al*[33]) showed an increase in Hct that was not statistically significant [63]. More importantly, Trivedi *et al*[33] directly compared fosinopril and theophylline and showed a statistically significant difference in terms of change in Hgb (baseline to three months 2.8 ± 1.7 *vs* -0.7 ± 0.69 gm/dL; P = 0.017) and Hct (baseline to three months 9.0 ± 6.0 *vs* -2.3 ± 2.7% P = 0.027). Notably, almost half (44.4%) of the theophylline arm dropped out of the study due to medication intolerance, consistent with other literature describing theophylline's narrow therapeutic index[3,25]. Further supporting this observation of ACE-I/ARB compared to theophylline is the study from Ok *et al*[25]. After a month washout period, they treated the KTRs randomized to theophylline with 10 mg of enalapril and saw improvement in mean Hct at 2 months (pre-treatment Hct 55% ; range = 52-64) *vs* post-treatment Hct (46% ; range = 40-53) and 3 months (post-treatment Hct 41%; range = 33-47)[25]. These studies are summarized in Table 3.

As a final line of therapy for patients who prefer to avoid both phlebotomy and theophylline, patients can have their antiproliferative immunosuppressive agent switched from mycophenolate to sirolimus, as PTE was found to be less prevalent in patient who were administered the latter agent[48]. However, sirolimus is associated with significant adverse effects precluding its use more commonly. It has a high incidence of side effects, namely stomatitis, proteinuria, hyperlipidemia, impaired wound healing, and interstitial pneumonitis[65].

In brief, several studies have shown that ACE-I/ARBs are first-line therapy, phlebotomy is second-line, and that theophylline is a limited alternative both in terms of efficacy and tolerance.

Additionally, while low dose aspirin is a commonly used agent for primary prevention for heart disease in KTRs, it has also been shown to reduce venous thromboembolism (VTE) events in patients with polycythemia vera[2]. However, there

Table 3 Effect on hemoglobin and hematocrit after use of theophylline

Ref.	Number of patients	Hgb pre	Hgb post	*P* value	Hct pre	Hct post	*P* value	Drug (mg/d)	Duration (wk)
Bakris *et al*[61], 1990	8				58	46	< 0.05	Theophylline	8
Grekas *et al*[62], 1995	8				58	50	< 0.05	Theophylline 600	8
Ok *et al*[25], 1995	9				56	52	NA	Theophylline 600	8
Yagisawa *et al*[63], 1996	1				50.3	53.5	NA	Theophylline	4
Trivedi *et al*[33], 2003	5	17.4 ± 0.7	18.1 ± 0.9	> 0.05	52.4 ± 2.7	54.7 ± 3.9	> 0.05	Theophylline	12

Hgb: Hemoglobin; Hct: Hematocrit; NA: Not available.

have been no studies to evaluate its use in patients with PTE and the benefit in these patients is unclear[14]. As such, its role for use solely in the context of PTE is unknown.

OUTCOMES

Due to the nature of PTE and higher blood viscosity, PTE has usually been associated with increased risk of stroke and both arterial and venous thromboembolic disease (such as PE, DVT, and myocardial infarction)[66,67]. Older studies have corroborated this finding, with VTE events having occurred among 18.9% of patients with PTE in earlier decades[43]. However, the risk of these complications has decreased in recent years.

In our recently published study of KTRs with PTE at our institution (n = 214), PTE was not associated with patient mortality (HR = 0.99, 95%CI: 0.69-1.42, P = 0.97), graft failure (HR = 1.11, 95%CI: 0.68-1.80, P = 0.69), or VTE (HR = 1.07, 95%CI: 0.59-1.96, P = 0.81)[41].

In short, poor outcomes related to post transplant erythrocytosis have lessened over time due to earlier diagnosis and improvement management with ACE-I/ARBs.

CONCLUSION

PTE occurs in 8%-15% of KTRs with a clear decline in recent decades. The majority of cases occur 8-24 months post-transplant presenting as either mild malaise, fatigue, or severe thromboembolic events. Males, patients without anemia pre-transplant, renal artery stenosis, patients with long pre-transplant dialysis courses, and stronger functioning grafts are known to be risk factors for acquiring PTE. An adequate workup for PTE should include ruling out hemoconcentration and secondary causes of erythrocytosis including renal artery stenosis, hypoxic lung disease, OSA, and malignancy. Current standard of treatment is use of ACE-I or ARB which have been found to be the most effective and best tolerated therapeutic option that it also thought to be the driving force of decreasing prevalence of PTE. Fortunately, recent studies have shown that the PTE does not negatively affect patient or graft survival and does not lead to higher rates of VTE.

In this review, we have appraised current literature to describe PTE in hopes of providing a framework for recognition and management of this disease, as well as providing a basis for further research and inquiry.

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