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Title: Cost savings with a novel algorithm for early detection of systemic sclerosis-related pulmonary arterial hypertension: alternate scenario analyses

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Abstract

Pulmonary Arterial Hypertension (PAH) is an important cause of death and disability in Scleroderma (SSc) patients. Yearly screening of all SSc patients with transthoracic echocardiography (TTE) is recommended in international guidelines and currently utilised by the Australian Scleroderma Interest Group ($ASIG_{STANDARD}$). Due to the limitations of TTE, the Australian Scleroderma Interest Group (ASIG) developed a new screening algorithm ($ASIG_{PROPOSED}$) utilizing a serum biomarker, NT-proBNP, in place of TTE, which has been shown to be equally accurate as the current algorithm. The aim of this study was to compare the cost of these two algorithms. The new algorithm resulted in significant yearly cost savings of between AUD$42,913.35 and AUD$84,570 in screening and diagnosis of the ASCS cohort which, if extrapolated to the Australian population, would result in a yearly cost saving of between AUD$367,066 and AUD$725,564. There was no scenario in which the proposed algorithm did not result in a cost saving.

Introduction

Systemic sclerosis (SSc) is a multisystem disease characterised by inflammation and fibrosis. Pulmonary arterial hypertension (PAH) is a leading cause of death in SSc, affecting approximately 12% of patients(1). Recent advances in therapy for PAH delay disease progression, reduce hospitalisations and improve survival (2, 3) and there is evidence that earlier detection of PAH and initiation of treatment has beneficial effects on functional capacity and survival(4, 5). However, early detection of PAH can be challenging as the disease is often clinically silent early in its course, eventually presenting with non-specific symptoms of dyspnoea, fatigue and decreased exercise tolerance, at which time there has already been substantial loss of pulmonary vascular reserve. Regular screening has been shown to detect PAH in patients earlier than in the course of routine clinical practice(6), which has led to the recommendation for annual screening for all patients with SSc.

The current screening recommendations consist of annual transthoracic echocardiography (TTE) and pulmonary function tests (PFTs), with patients who screen positive referred for right heart catheterisation (RHC). However, as a screening tool, TTE has significant limitations(7). It can be costly in terms of resources and financially, is dependent on operator technique and is unable to estimate systolic pulmonary artery pressure (sPAP) in up to 30% of patients due to lack of a tricuspid regurgitant jet(8). Further, access to good quality echocardiography for estimation of sPAP is very limited in regional Australia, with prolonged waiting times in many metropolitan areas. In an effort to reduce the reliance on TTE, the Australian Scleroderma Interest Group (ASIG) has developed an alternative algorithm for the yearly screening of patients with SSc, involving PFTs and a serum biomarker, NT pro-BNP, as first tier screening tests for PAH(9). NT pro-BNP, is released by cardiac myocytes under stress and has been shown to correlate with NYHA functional class,

exercise capacity and haemodynamics in SSc-PAH(10). The new algorithm has been shown to be equally, if not more, sensitive and specific than the current guidelines with a negative predictive value (NPV) of 100%(11).

In addition to improved accuracy and accessibility, the new algorithm has also been shown to result in cost savings in the Australian context based on the Medicare Benefit Schedule (MBS), both in the initial year of screening and in subsequent years(12). This study showed a cost reduction of $931, 535 for screening of all Australians with SSc in the initial year of screening and in subsequent years of screening, the new algorithm resulted in a cost saving of $838, 381. 50 per year. A limitation of this study was that a number of assumptions were made, with regard to the disease prevalence and negative predictive value (NPV) of the algorithm, in order to calculate screening costs in subsequent years. The aim of the present study is to compare the costs of the current and proposed screening algorithms using a range of NPV for the algorithms and also a range of prevalence of positive screens.

Methods

643 consecutive patients from the Australian Scleroderma Cohort Study (ASCS) were included in this analysis. All patients underwent screening using the current ASIG screening guidelines ($ASIG_{STANDARD}$) and the proposed NT-proBNP based screening algorithm ($ASIG_{PROPOSED}$).

A positive screen in the current algorithm ($ASIG_{STANDARD}$) is defined as a sPAP $\geq$40mmHg on TTE or DLCO<50% predicted with forced vital capacity (FVC) > 85% predicted on PFTs. A positive screen using the new algorithm ($ASIG_{PROPOSED}$) requires one of the following criteria to be fulfilled: either DLCO <70% predicted with FVC/DLCO ratio ≥1.8 on PFT or an NT-proBNP level ≥210 pg/ml. For the purposes of this analysis, we assumed that all patients who screened positive using NT- proBNP and PFTs underwent TTE. It was assumed that both algorithms were equally sensitive and specific for the purposes of this analysis and that all positive screens in both algorithms underwent confirmatory RHC. The cost of RHC was therefore included in the cost of diagnosis, but not in the cost of screening.

The costs of each screening algorithm were modeled for each subsequent year of screening. The calculations were performed using a range of positive screens, the number of positive screens in our initial cost paper (36%) and two lower values if the algorithm were to be applied in a population where SSc-PAH is less prevalent (20% and 5%) and a range of NPV (100%, 90%, 80%). After removing the patients who would have screened positive in the first year of screening (based on a prevalence of PAH of 12% in SSc) the number of patients remaining was between 566 and 582 depending on the assumed NPV of the algorithm. Two scenarios were used in this analysis. In Scenario 1, it was assumed that all positive screens in both algorithms

would undergo TTE every year. In reality however, as TTE was completed in the initial year of screening positive, it may not be necessary in every subsequent year of screening positive. Therefore, in the second scenario (Scenario 2) it was assumed that only a proportion of positive screens would undergo TTE (based on incidence of PAH being 1.4% in SSc). These two scenarios provide the extreme ranges of cost, with the true cost likely between them. These costs were then extrapolated to estimate the cost of screening if both algorithms were applied to the entire population of SSc patients (approximately 5,500 patients) within Australia (13).

The costs of screening each patient were obtained from the most recent Medicare Benefits Schedule with the cost being AUD$196.10 for TTE, AUD$117.90 for PFTs and AUD$49.75 for NT-proBNP. The cost of screening a single patient using the current algorithm, consisting of PFTs and TTE is AUD$314, whilst the proposed algorithm, consisting of PTFs and NT pro-BNP costs AUD$167.65. If patients screened positive in the first scenario, they would then proceed to TTE at a cost of AUD$196.10 which was included in the total cost of screening. The cost of diagnosis included the cost for screening and the cost of RHC for positive screens, being AUD$4, 943.65.

Results

In Scenario 1 (all positive screens undergoing TTE), the proposed algorithm reduced the yearly cost of screening and diagnosis by 4-24% (depending on the number of positive screens and subsequent TTEs), amounting to a cost saving of between $42, 913.35 and $79, 440.02 in the ASCS cohort (see table 1). If these values were extrapolated to the Australian SSc population the cost savings per year would be between $367, 066.01 and $679, 503.42. The cost to diagnose one case of PAH in the ASCS cohort was reduced by between $5,411 (at the most conservative estimate) to $12, 520.867 per year.

In Scenario 2 (TTE performed only in the first year of a positive screen), the proposed algorithm resulted in a 7-26% reduction in the cost of screening amounting to a cost saving of between $82, 120 and $84, 570 in the ASCS cohort (see table 1). If these values were extrapolated to the Australian SSc population, the cost savings per year would be between $702, 429 and $725, 564. The cost to diagnose one case of PAH in this scenario was reduced by between $10, 382.98 and $13, 370. There was no scenario in which the proposed algorithm did not result in cost saving.

Discussion

Yearly screening for SSC-PAH is recommended in all SSc patients and this study has demonstrated that the proposed algorithm results in significant cost savings at a range of frequencies of positive screens and NPV.

The two scenarios described above provide a range of values for the estimated cost savings, with the real value likely to lie between them (see table 1). We know from previous published studies by our group that a substantial proportion of those who screen positive with the existing TTE based algorithm do not undergo RHC(1). However, this does not necessarily reflect best practice, and may in fact reflect lack of confidence in interpreting the results of TTE-based screening, or lack of access to RHC. In calculating potential cost savings with the new versus existing algorithm, we have made the most conservative assumption that all patients who screen positive with either algorithm will undergo RHC.

In this analysis, we assumed that all patients who screened positive would undergo RHC in order to calculate the maximum possible cost encountered. In reality however, for patients who have a positive screen and undergo RHC in the first year of screening, wherein PAH according to international criteria is not found, the decision to repeat RHC in subsequent years is made on an individual case basis. While it is recommended that all SSc patients should continue to undergo annual screening, in situations where the screen remains positive, the decision to repeat RHC will depend on the magnitude change in NT-proBNP level and pulmonary function tests, and the findings on TTE and previous RHC.

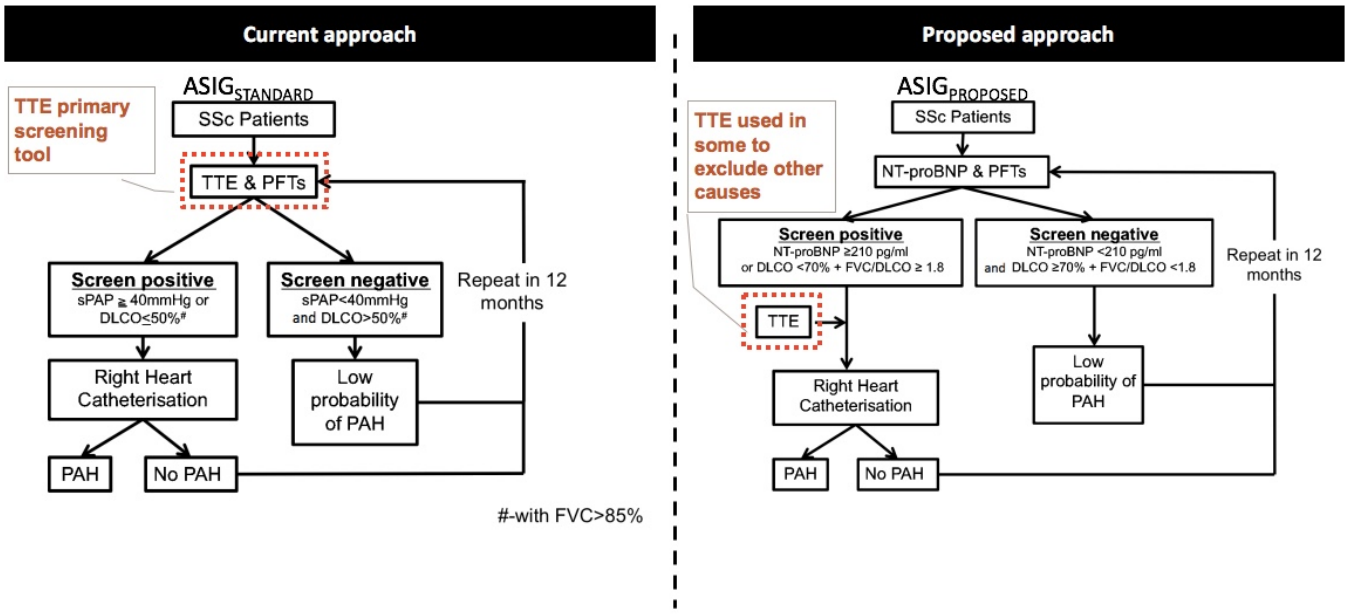
For an annual PAH screening program to be cost-effective, it should be highly sensitive and sufficiently specific, be affordable, easy to implement and accessible to everyone. The current screening algorithm relies heavily on TTE, which has many limitations even when taking into account more recent 2015 guidleines to improve accuracy(14). While in addition to RVSP and peak tricuspid regurgitant velocity, there are other parameters such as pulmonary artery diameter or right atrial area that may be assessed at no additional cost, these are not routinely reported in all TTE. Furthermore, TTE for investigation of PAH requires specific expertise in assessment of right heart pressures and structures that is not available in all centres. An NT-proBNP based model for PAH screening shifts reliance from TTE for which the required expertise may not be available in all centres.

The new algorithm improves the affordability and accessibility of screening, while having similar performance characteristics (sensitivity and specificity) as previously shown. In practice, the greater accessibility is of particular value, especially to those in rural settings, and has the potential to improve adherence to screening recommendations. Unfortunately, NT pro-BNP is not listed on the MBS for the diagnosis of PAH, with the only approved use being in an emergency department for the differentiation of dyspnoea due to cardiac or respiratory causes. However, the cost savings presented in this paper make a strong case for the listing of NT pro-BNP on the MBS for screening of PAH in SSc patients.

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Figure 1. Current ($ASIG_{STANDARD}$) and proposed ($ASIG_{PROPOSED}$) approaches to screening for SSc PAH



Abbreviations: $ASIG_{STANDARD}$ = Australian Scleroderma Interest Group standard SSc-PAH screening algorithm; : $ASIG_{PROPOSED}$ = Australian Scleroderma Interest Group proposed SSc-PAH screening algorithm; DLCO= Diffusion Capacity; FVC= Forced Vital Capacity; PAH= Pulmonary Arterial Hypertension; PFTs= Pulmonary Function Tests; SSc= Systemic sclerosis; TTE= Transthoracic echocardiography.

Table 1- Absolute costs and differences in cost of screening and diagnosis with $ASIG_{STANDARD}$ versus $ASIG_{PROPOSED}$ per year #

Scenario 1*	ASIG Standard	ASIG Proposed	Difference	% Difference
ASCS Population				
No. of TTE performed	574	117	363-533	64-95%
Cost of screening and diagnosis	$317,900-$1,186,053	$240,549-$1,174,021	$42,913 -$79,440	4-24%
Cost per diagnosis				
No. of TTE to diagnose one case of PAH	71-92	4-33	46-87	64-95%
Cost to diagnose one case of PAH	$40,084-$191,988	$30,331-$109,633	$5,411 -$12,521	4%-24%
Australian SSc population				
No. of TTE performed	4,846-4,976	242-1792	3101-4728	64-95%
Total cost of screening and diagnosis	$2,719,209-$10,419,158	$2,057,581-$10,042,176	$367,066 -$679,503	4-43%
Scenario 2**	**ASIG Standard**	**ASIG Proposed**	**Difference**	**% Difference**
ASCS Population				
No. of TTE performed	566-582	3-4	562-579	99%
Cost of screening and diagnosis	$317,900-$1,186,053	$235,780-$1,103,708	$82,120-$84,570	7-26%
Cost per diagnosis				
No. of TTE to diagnose one case of PAH	71-92	0	71-92	99%
Cost to diagnose one case of PAH	$40,084-$149,551	$29,640-$139,168	$10,383-$13,370	7-26%
Australian SSc population				
No. of TTE performed	4846-4976	24-34	4811-4962	99%
Total cost of screening and diagnosis	$2,719,209-$10,145,091	$2,016,708-$9,440,741	$702,429-$725,564	7-26%

Abbreviations: ASCS = Australian Scleroderma Cohort Study; $ASIG_{STANDARD}$ = Australian Scleroderma Interest Group standard SSc-PAH screening algorithm; $ASIG_{PROPOSED}$ = Australian Scleroderma Interest Group proposed SSc-PAH screening algorithm; FVC= Forced Vital Capacity; No. = Number; PAH= Pulmonary Arterial Hypertension; SSc= Systemic sclerosis; TTE= Transthoracic echocardiography.

* Assumed all positive screen underwent TTE

** Assumed that TTE is performed only in the first year of a positive screen

The costs of each screening algorithm were modeled for each subsequent year of screening with the actual costs and difference between the two algorithms shown. The calculations were performed using a range of frequencies for positive screens (36%, 20%, 5%) and a range of NPV (100%, 90%, 80%), and the minimum and maximum estimated costs calculated are presented in the table. The number of TTEs performed depended on the assumed range of positive screens (as only positive screens in the proposed algorithm would undergo TTE). The costs of screening each patient were obtained from the most recent Medicare Benefits Schedule and are expressed in AUD.
$ASIG_{STANDARD}$ consisted of yearly PFTs and TTE (total cost of AUD$314). $ASIG_{PROPOSED}$ consisted of yearly PFTs and NT pro-BNP (total cost of AUD$167.65). In scenario 1, a positive screen in $ASIG_{PROPOSED}$ alogorithm would proceed to TTE at an additional cost of AUD$196.10. All positive screens in both algorithms would proceed to diagnostic RHC (at a cost of AUD$4, 943.65). The cost of diagnosis included the cost for screening and the cost of RHC for positive screens.