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# Impact of Autologous Stem Cell Transplantation on Cardiac Involvement in Systemic Sclerosis

**Meer**

## Beyond Conventional Echocardiography

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CZECH CARDIOVASCULAR RESEARCH AND INNOVATION DAY 2024

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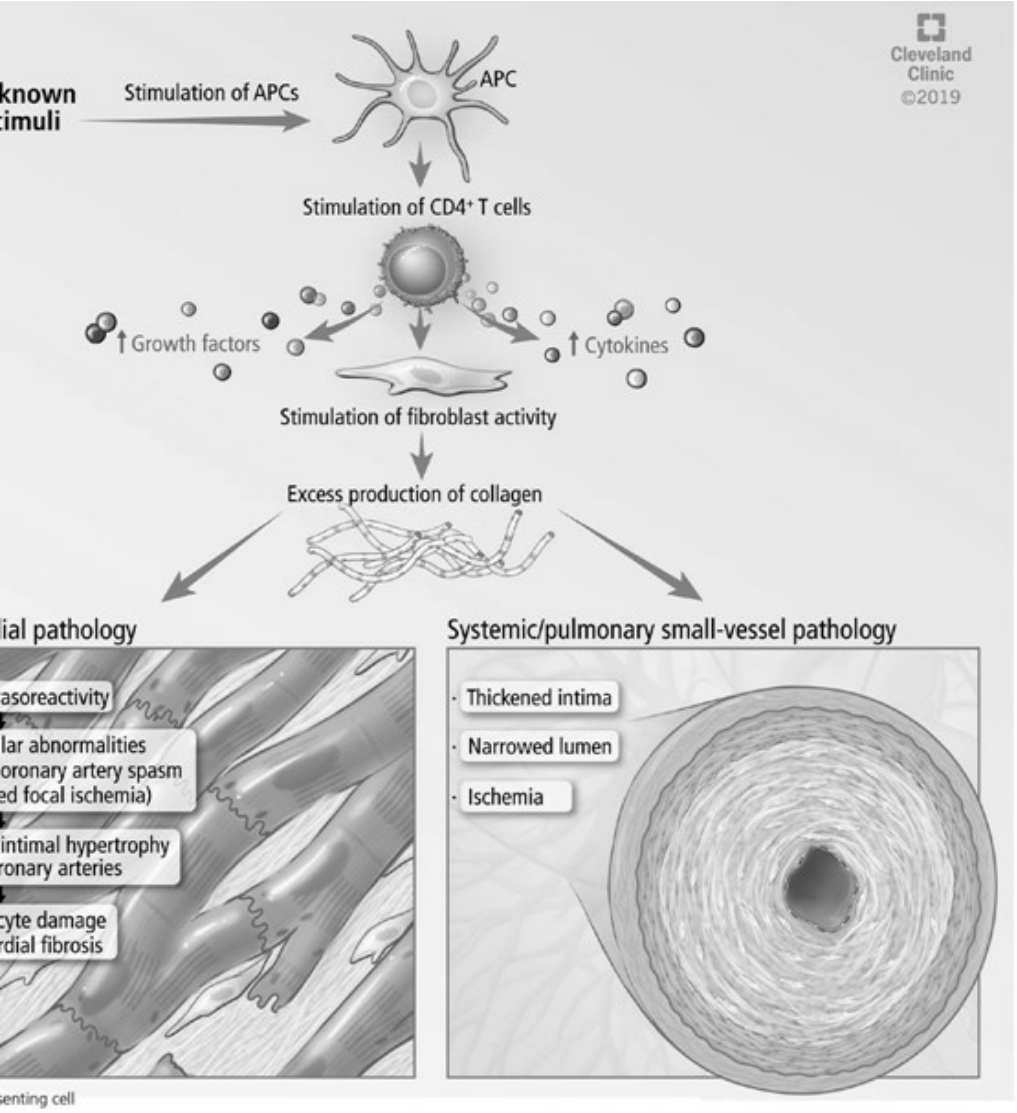
# GROUND




- Systemic Sclerosis (SSc): a rare connective tissue disorder characterized by progressive fibrosis of skin and various internal organs
- Cardiovascular involvement is highly prevalent in SSc
  - estimated prevalence of up to 35%
  - worsens prognosis with a mortality of 70% at 5 years
- **However**, cardiac impairment is often subclinical and often overlooked when assessed by conventional imaging methods


Tyndall et al. 2010; Elhai et al. 2012; Allanore et al. 2010

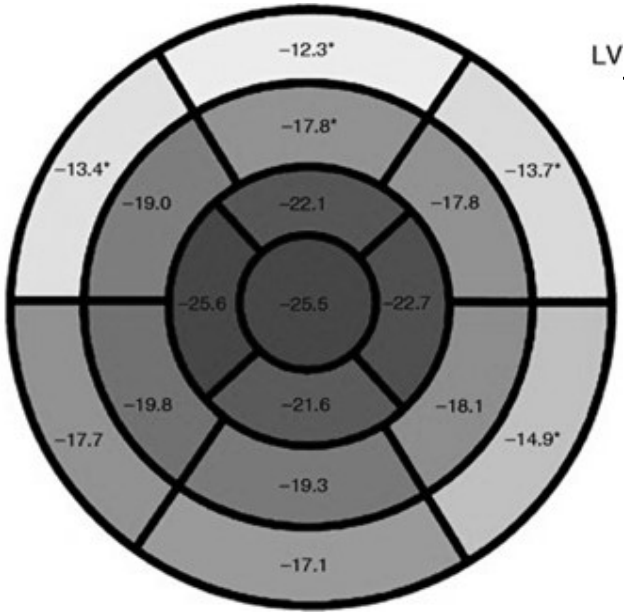



**Table 3 Left ventricular ejection fraction, pw DTI and speckle tracking strain data**

| | Baseline (n = 19) | Follow-up (n = 19) | *p*-value |
|---|---|---|---|
| LVEF, (%) | 63.3 ± 4.2 | 63.2 ± 5.0 | ns |
| Peak systolic velocity (cm/s) | 7.7 ± 1.5 | 7.8 ± 1.7 | ns |
| ***Longitudinal PSS*** | | | |
| Global longitudinal PSS, (%) | −22.0 ± 2.3 | −20.8 ± 2.1 | 0.04 |
| APLAX, (%) | −21.5 ± 3.5 | −20.3 ± 2.7 | ns |
| 4CH, (%) | −22.1 ± 2.5 | −19.8 ± 3.5 | 0.006 |
| 2CH, (%) | −22.2 ± 2.7 | −21.7 ± 2.6 | ns |

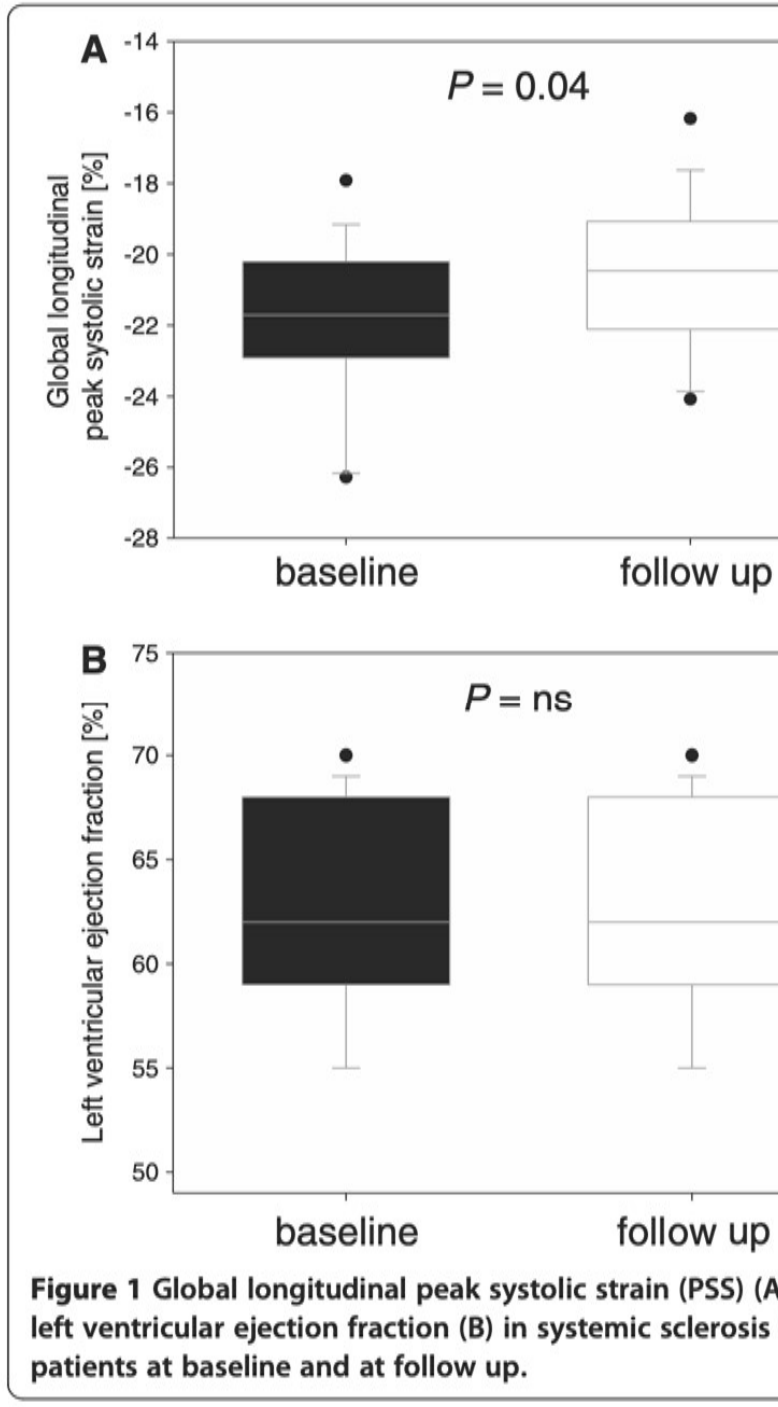
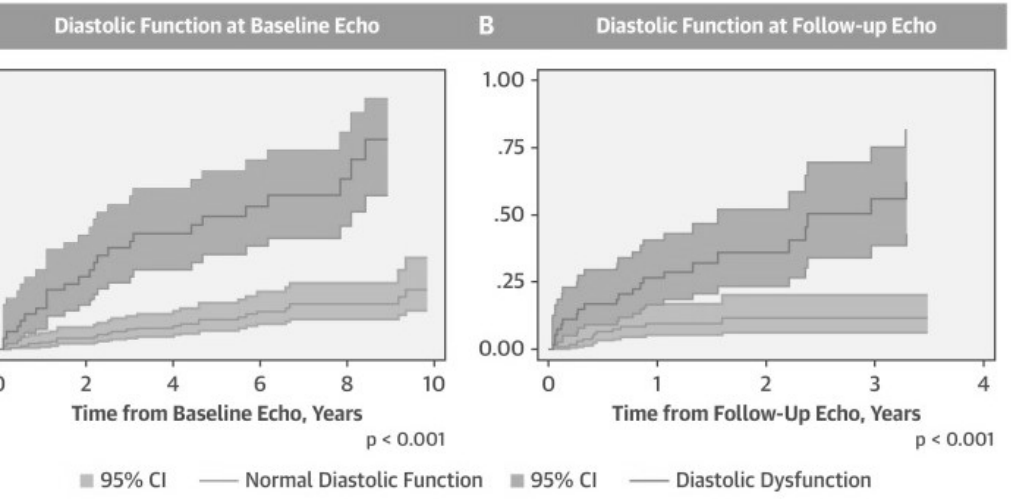



**Figure 1** Global longitudinal peak systolic strain (PSS) (A left ventricular ejection fraction (B) in systemic sclerosis patients at baseline and at follow up.



Guerra et al. 2018; Spethmann et al. 2014; van Wijngaarden et al. 2019

TRAL ILLUSTRATION: Diastolic Dysfunction-Related Mortality in Sys-
Sclerosis

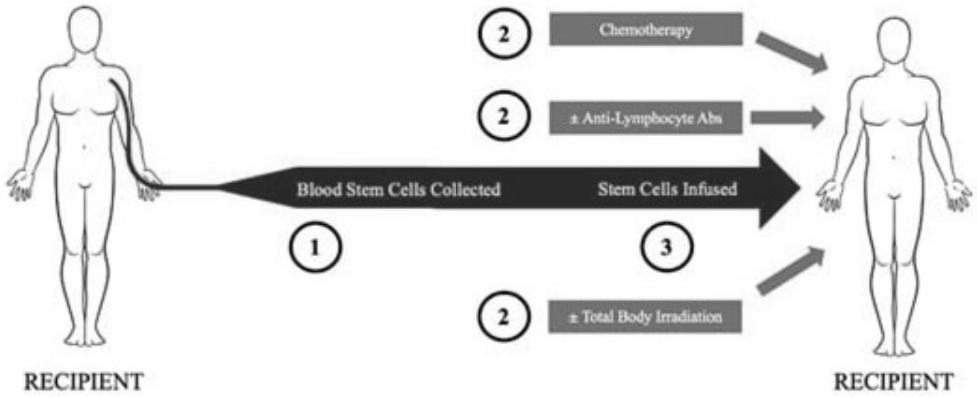


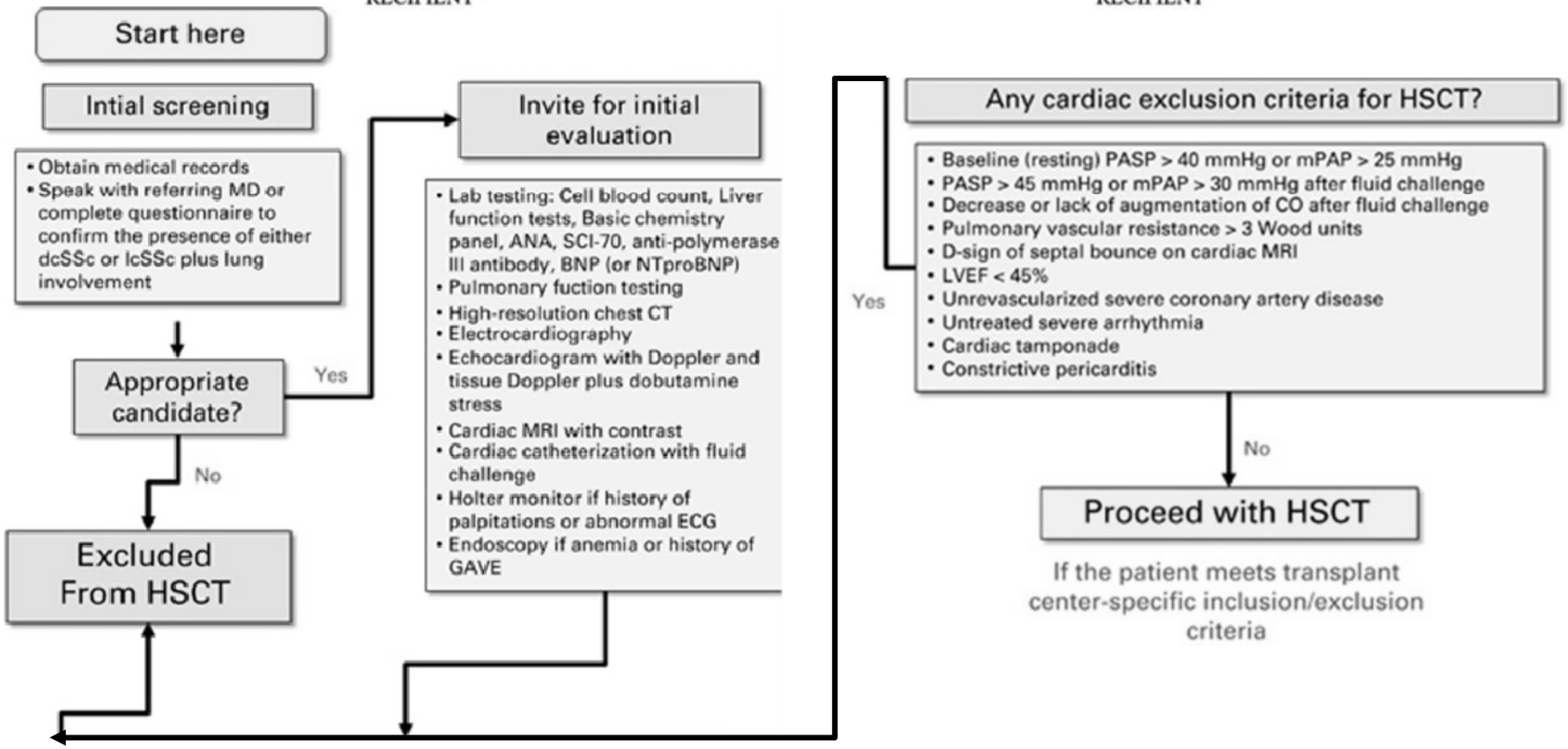

e, A.H. et al. J Am Coll Cardiol. 2018;72(15):1804-13.

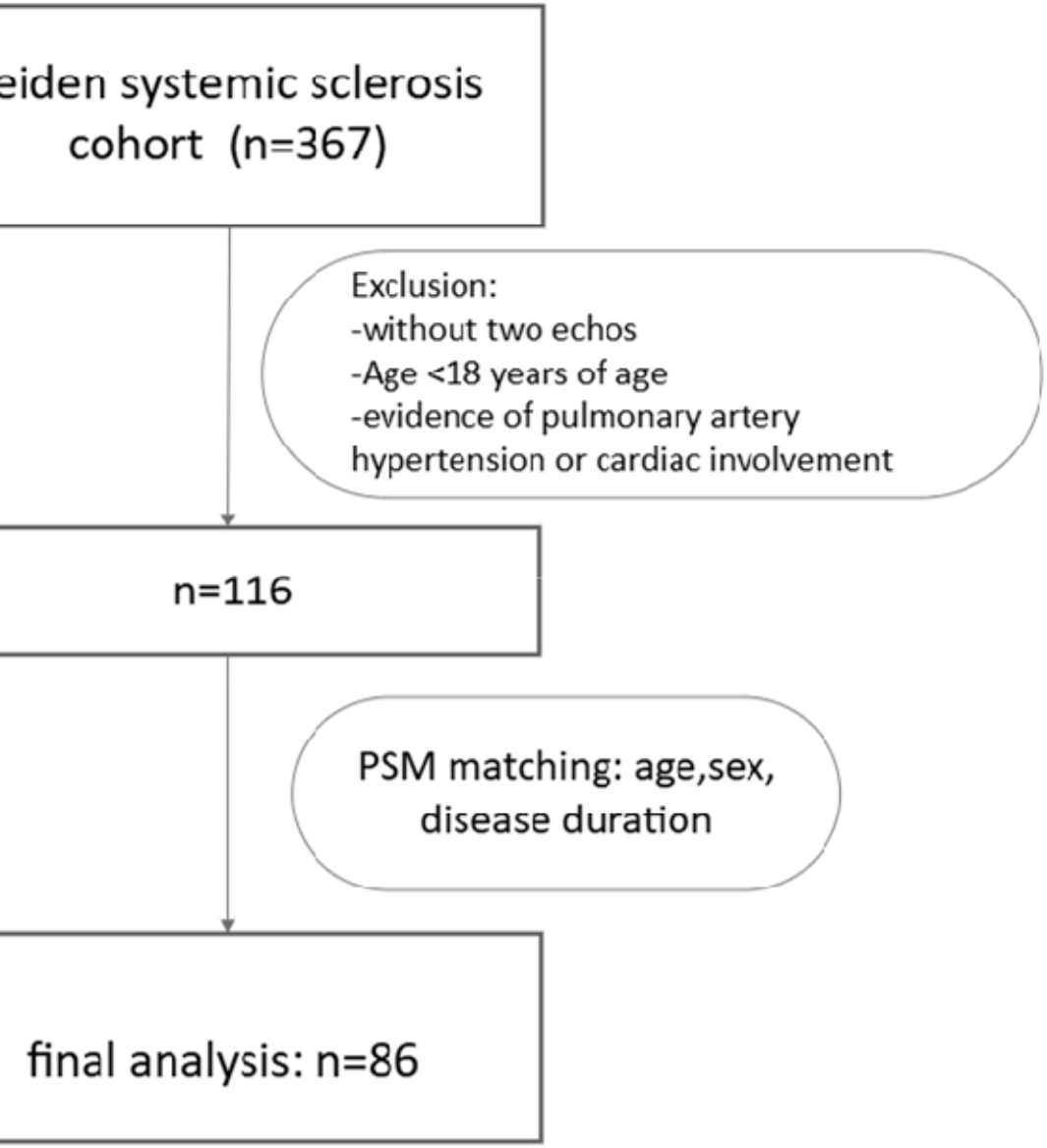
**TABLE 3 Prediction of Mortality by Multivariable Cox Regression**

| | Multivariable Cox Regression on Mortality | | |
|---|---|---|---|
| | HR | 95% CI | p Value |
| DD | 3.71 | 1.69-8.14 | 0.001 |
| DLCO, % | 0.96 | 0.94-0.98 | 0.001 |
| Age | 1.05 | 1.02-1.09 | 0.003 |
| Male | 1.23 | 0.54-2.80 | 0.624 |
| mRSS | 1.06 | 1.03-1.09 | <0.001 |
| TAPSE | 0.35 | 0.17-0.73 | 0.005 |
| NT-proBNP | 1.01 | 1.01-1.01 | 0.014 |
| C-index | | 0.89 | |

CI = confidence interval; DD = diastolic dysfunction; DLCO = diffusion capacity of the lung for carbon monoxide; HR = hazard ratio; mRSS = modified Rodnan skin score; NT-proBNP = N-terminal prohormone of brain natriuretic peptide; TAPSE = tricuspid annular plane systolic excursion.


2
Chemotherapy
2
± Anti-Lymphocyte Abs
Blood Stem Cells Collected
Stem Cells Infused
1
3
2
± Total Body Irradiation
RECIPIENT
RECIPIENT


Start here
Intial screening
• Obtain medical records
• Speak with referring MD or complete questionnaire to confirm the presence of either dcSSc or lcSSc plus lung involvement
Appropriate candidate?
Yes
No
Excluded From HSCT
Invite for initial evaluation
• Lab testing: Cell blood count, Liver function tests, Basic chemistry panel, ANA, SCI-70, anti-polymerase III antibody, BNP (or NTproBNP)
• Pulmonary fuction testing
• High-resolution chest CT
• Electrocardiography
• Echocardiogram with Doppler and tissue Doppler plus dobutamine stress
• Cardiac MRI with contrast
• Cardiac catheterization with fluid challenge
• Holter monitor if history of palpitations or abnormal ECG
• Endoscopy if anemia or history of GAVE
Any cardiac exclusion criteria for HSCT?
Yes
• Baseline (resting) PASP > 40 mmHg or mPAP > 25 mmHg
• PASP > 45 mmHg or mPAP > 30 mmHg after fluid challenge
• Decrease or lack of augmentation of CO after fluid challenge
• Pulmonary vascular resistance > 3 Wood units
• D-sign of septal bounce on cardiac MRI
• LVEF < 45%
• Unrevascularized severe coronary artery disease
• Untreated severe arrhythmia
• Cardiac tamponade
• Constrictive pericarditis
No
Proceed with HSCT
If the patient meets transplant center-specific inclusion/exclusion criteria




Primary outcome

- absolute values and relative longitudinal changes in systolic (LVEF and LV-GLS)

Secondary outcome

- diastolic (E/A, E/e', TRV and LAVI) function parameters

Statistical Analysis

- The association between ASCT and echocardiographic changes over time was assessed using linear mixed-effect regress models, with random intercept to account inter-individual effects and within-subject correlations as a result of repeated measurements.

| Table 1 | Non-ASCT (n = 43) | ASCT (n = 43) | P value |
|---|---|---|---|
| Age, yrs | 44.91 (11.14) | 43.23 (9.89) | 0.463 |
| Female | 13 ( 36.1) | 21 ( 48.8) | 0.363 |
| BMI, kg/m$^2$ | 22.37 (3.16) | 24.80 (2.80) | 0.001 |
| Disease duration, yrs | 1.0 [0.2, 3.6] | 0.0 [0.0, 5.0] | 0.355 |
| ATA | 18 ( 50.0) | 24 ( 55.8) | 0.772 |
| ANA | 35 ( 97.2) | 40 ( 93.0) | 0.739 |
| ACA | 5 ( 13.9) | 0 ( 0.0) | 0.039 |
| mRSS | 10.7 (9.1) | 13.4 (12.1) | 0.279 |
| Digital ulcers | 4 ( 11.4) | 2 ( 4.9) | 0.529 |
| Muscle weakness | 3 ( 8.6) | 4 ( 9.8) | 1.000 |
| lung fibrosis | 3 ( 9.4) | 2 ( 4.9) | 0.773 |
| Never-smoker | 26 ( 81.2) | 35 ( 85.4) | 0.879 |
| Hypertension | 6 ( 20.7) | 4 ( 10.5) | 0.418 |
| FVC, % | 95.37 (19.81) | 88.76 (20.83) | 0.169 |
| DLCO, % | 60.59 (33.58) | 61.76 (19.85) | 0.852 |

| Table 2 | Non-ASCT (n = 43) | ASCT (n = 43) | P value |
|---|---|---|---|
| LVEDV, ml | 96.58 (33.66) | 102.73 (30.14) | 0.462 |
| LVESV, ml | 39.36 (19.14) | 41.42 (15.64) | 0.654 |
| LVEF, % | 56,11 (6,35) | 52,55 (9,09) | 0.044 |
| LVGLS, % | -19,50 (2,53) | -18,04 (2,59) | 0,014 |
| IVST, mm | 9.61 (2.14) | 9.42 (2.02) | 0.728 |
| PWT, mm | 9.17 (1.99) | 9.42 (1.88) | 0.611 |
| LAVI, ml/m² | 25.70 (9.66) | 30.52 (9.91) | 0.056 |
| E/e' | 8.23 (2.42) | 7.83 (2.18) | 0.473 |
| e', cm/s | 9.63 (2.71) | 9.45 (2.70) | 0.746 |
| E/A | 1.27 (0.34) | 1.23 (0.32) | 0.642 |
| TRV, cm/s | 2.22 (0.54) | 2.17 (0.48) | 0.726 |
| Diastolic Dysfunction (%) | | | |
| I | 34 ( 94.4) | 34 ( 91.9) | 0.611 |
| II | 2 ( 5.6) | 2 ( 5.4) | |
| III | 0 ( 0.0) | 1 ( 2.7) | |

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# LT: Longitudinal changes

| | Non-ASCT (n = 43) | ASCT (n = 43) | Difference between groups (95% CI) | P value |
|---|---|---|---|---|
| EA at baseline (%) | 1.28 [1.18, 1.39] | 1.22 [1.11, 1.33] | 0.060 (-0.092, 0.21) | 0.438 |
| EA at 1 year (%) | 1.25 [1.13, 1.36] | 1.18 [1.07, 1.29] | 0.063 (-0.090, 0.22) | 0.418 |
| EA at 2 years (%) | 1.20 [1.08, 1.31] | 1.16 [1.05, 1.27] | 0.037 (-0.12, 0.20) | 0.642 |
| EA at 3 years (%) | 1.15 [1.03, 1.26] | 1.12 [1.01, 1.23] | 0.022 (-0.13, 0.18) | 0.778 |

# LT: Longitudinal changes

| | Non-ASCT (n = 43) | ASCT (n = 43) | Difference between groups (95% CI) | P value |
|---|---|---|---|---|
| e' at baseline (m/s) | 10.06 (9.34, 10.77) | 10.21 (9.45, 10.96) | -0.15 (-1.17, 0.88) | 0. 778 |
| e' at 1 year (m/s) | 10.14 (9.39, 10.90) | 9.41 (8.68, 10.14) | 0.73 (-0.30, 1.76) | 0.162 |
| e' at 2 years (m/s) | 9.93 (9.17, 10.69) | 9.60 (8.85, 10.35) | 0.33 (0.73, 1.39) | 0.539 |
| e' at 3 years (m/s) | 9.38 (8.62, 10.13) | 9.24 (8.50, 9.98) | 0.14 (-0.90, 1.17) | 0.795 |

# LT: Longitudinal changes

| | Non-ASCT (n = 43) | ASCT (n = 43) | Difference between groups (95% CI) | P value |
|---|---|---|---|---|
| TRV at baseline (m/s) | 2.19 [2.05, 2.33] | 2.13 [1.98, 2.28] | 0.057 (-0.15, 0.26) | 0.586 |
| TRV at 1 year (m/s) | 2.15 [2.01, 2.30] | 2.13 [1.99, 2.28] | 0.020 (-0.18, 0.22) | 0.843 |
| TRV at 2 years (m/s) | 2.15 [2.00, 2.30] | 2.20 [2.05, 2.35] | -0.047 (-0.26, 0.16) | 0.662 |
| TRV at 3 years (m/s) | 2.24 [2.09, 2.38] | 2.21 [2.07, 2.36] | 0.021 (-0.19, 0.23) | 0.841 |

# LT: Longitudinal changes

| | Non-ASCT (n = 43) | ASCT (n = 43) | Difference between groups (95% CI) | P value |
|---|---|---|---|---|
| E/e' at baseline (%) | 8.46 [7.84, 9.09] | 7.88 [7.21, 8.54] | 0.589 (-0.32, 1.50) | 0.204 |
| E/e' at 1 year (%) | 7.18 [6.51, 7.84] | 7.47 [6.83, 8.12] | -0.297 (-1.22, 0.63) | 0.527 |
| E/e' at 2 years (%) | 7.71 [7.03, 8.38] | 7.19 [6.52, 7.85] | 0.520 (-0.42, 1.46) | 0.278 |
| E/e' at 3 years (%) | 7.39 [6.73, 8.06] | 7.49 [6.83, 8.14] | -0.091 (-1.02, 0.84) | 0.846 |

# LT: Longitudinal changes

| | Non-ASCT (n = 43) | ASCT (n = 43) | Difference between groups (95% CI) | P value |
|---|---|---|---|---|
| LAVI at baseline (ml/m2) | 25.2 [22.5, 27.9] | 30.1 [27.4, 32.8] | -4.86 [-8.68, -1.05] | 0.013 |
| LAVI at 1 year (ml/m2) | 26.1 [23.3, 29.0] | 26.9 [24.3, 29.6] | -0.82 [-4.66, 3.03] | 0.676 |
| LAVI at 2 years (ml/m2) | 22.8 [19.9, 25.7] | 28.0 [25.3, 30.7] | -5.22 [-9.13, -1.31] | 0.009 |
| LAVI at 3 years (ml/m2) | 24.1 [21.2, 26.9] | 26.1 [23.5, 28.8] | -2.06 [-5.91, 1.79] | 0.293 |

## CLUSION

n SSc patients, ASCT showed a favorable impact on LV systolic function.

The study suggests that ASCT significantly benefits SSc patients in terms of LV systolic function, evidenced by improvements in LVEF and LV-GLS over time. This finding also highlights the role of LV-GLS as a potential marker for monitoring myocardial response to this treatment, making it a valuable tool in clinical practice for assessing cardiac damage and treatment efficacy in SSc patients undergoing ASCT.