Transient effect of iloprost on left ventricular global longitudinal strain in systemic sclerosis

Sirs,

Systemic sclerosis (SSc) is characterised by diffuse microangiopathy, which plays a central role in myocardial involvement, often subclinical and difficult to detect with conventional echocardiography (1). Global longitudinal strain (GLS) is a sensitive marker of early systolic dysfunction and is frequently reduced in SSc despite preserved ejection fraction (2). Given the central role of microvascular dysfunction, vasoactive therapies may represent a modifiable target for myocardial impairment.

Prostacyclin analogues, such as iloprost, are widely used in SSc for peripheral vascular manifestations (3). In a previous proof-of-concept study, we demonstrated that intravenous iloprost acutely improves GLS, suggesting a rapid enhancement of myocardial contractility, likely mediated by improved microvascular perfusion (4). However, whether this effect is transient or sustained remained unclear.

To address this, we conducted a prospective observational study including 21 consecutive SSc patients (mean age 52.9±13.1 years; 18 females) undergoing intravenous iloprost for digital ulcers or severe Raynaud's phenomenon. All patients fulfilled 2013 ACR/EULAR classification criteria (5). Transthoracic echocardiography with GLS assessment was performed at baseline, immediately after a 6-hour iloprost infusion, and at 2-week follow-up. Methodological details have been previously described (4, 6).

At baseline, GLS values were reduced in most patients, confirming the presence of subclinical myocardial dysfunction (7). Iloprost infusion induced a significant improvement in GLS (Fig. 1), particularly in the apical four-chamber view (from -13.2±2.1 to -15.2±2.9; p=0.007). When considering GLS derived from all apical views, the improvement remained statistically significant (from -13.4±2.5 to -15.9±3.5; p=0.045). Notably, no significant changes were observed in blood pressure or heart rate, suggesting that the GLS improvement was not driven by systemic hemodynamic variations.

However, at 2-week follow-up, GLS values returned to baseline levels (-13.4±2.5 *vs.* -13.7±3.5; n.s.), indicating that the observed effect was not maintained over time. No correlation was found between GLS changes and clinical or disease-related parameters. These findings support the interpretation that the improvement in myocardial deformation reflects a direct and short-lived pharmacological effect rather than a sustained modification of myocardial function.

The transient nature of this effect has relevant pathophysiological and clinical implications. It reinforces the concept that myocardial dysfunction in SSc is strongly influenced by dynamic microvascular factors, which can be acutely modulated but are not durably corrected by intermittent prostacyclin administration. While iloprost appears capable of temporarily enhancing myocardial performance, likely through improved microvascular perfusion and oxygen delivery, this does not translate into persistent functional benefit under standard treatment regimens.

This interpretation is consistent with emerging data suggesting that continuous or long-term vasodilatory strategies may be required to influence cardiac outcomes. In this regard, Guédon *et al*. reported that long-term sildenafil therapy, but not iloprost, was associated with a reduced incidence of diastolic dysfunction in SSc, supporting the hypothesis that sustained microvascular modulation is necessary to impact disease progression (8).

From a clinical perspective, our findings suggest the existence of a "functional-pharmacological window" in which myocardial performance can be transiently improved. Although speculative, this raises the possibility that iloprost could be beneficial in selected acute settings characterised by increased microvascular stress (9). However, such applications require dedicated investigation.

This study has limitations, including the small sample size, single-centre design, and lack of a control group. Nevertheless, it provides consistent evidence that iloprost-induced improvement in GLS is reversible and short-lived.

In conclusion, intravenous iloprost induces a significant but transient improvement in left ventricular myocardial deformation in SSc patients. This effect is not maintained at short-term follow-up, indicating a predominantly pharmacological and non-disease-modifying action on myocardial contractility.

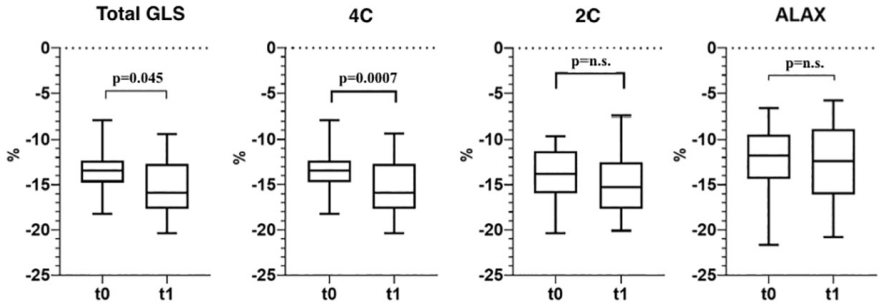

Fig. 1. Comparison between the mean global longitudinal strain (GLS) before and after iloprost administration in SSc patients. On the left, the box plot shows a significant improvement of the GLS obtained from the integration of the GLS calculated in the 4-chambers (4c), two-chambers (2c), and long axis (ALAX) views. The more significant improvement was obtained from the 4c view.

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References

1. BRUNI C, ROSS L: Cardiac involvement in systemic sclerosis: getting to the heart of the matter. *Best Pract Res Clin Rheumatol* 2021; 35(3): 101668. https://doi.org/10.1016/j.berh.2021.101668
2. TSCHÖPE C, SENNI M: Usefulness and clinical relevance of left ventricular global longitudinal systolic strain in patients with heart failure with preserved ejection fraction. *Heart Fail Rev* 2020; 25(1): 67-73. https://doi.org/10.1007/s10741-019-09853-7
3. POPE JE, DENTON CP, JOHNSON SR, FERNANDEZ-CODINA A, HUDSON M, NEVSKAYA: State-of-the-art evidence in the treatment of systemic sclerosis. *Nat Rev Rheumatol* 2023; 19(4): 212-26. https://doi.org/10.1038/s41584-023-00909-5
4. ISAIA I, APARO P, CASTELLETTI F *et al.:* Evaluation of changes in cardiac longitudinal strain rate in patients with systemic sclerosis undergoing iloprost treatment: an observational study. *Rheumatology* 2025; 64(5): 3063-68. https://doi.org/10.1093/rheumatology/keae441
5. VAN DEN HOOGEN F, KHANNA D, FRANSEN J *et al.:* 2013 classification criteria for systemic sclerosis: an American College of Rheumatology/European League against Rheumatism Collaborative Initiative. *Ann Rheum Dis* 2013;7 2(11): 1747-55. https://doi.org/10.1136/annrheumdis-2013-204424
6. SMISETH OA, RIDER O, CVIJIC M, VALKOVIČ L, REMME EW, VOIGT JU: Myocardial strain imaging: theory, current practice, and the future. *JACC Cardiovasc Imaging* 2025; 18(3): 340-81. https://doi.org/10.1016/j.jcmg.2024.07.011
7. CASIAN M, DIMA A, JURCUŢ C *et al.:* Cardiac function and mechanics in systemic sclerosis: a systematic review and meta-analysis. *Echo Res Pract* 2025; 12(1): 18. https://doi.org/10.1186/s44156-025-00081-4
8. GUÉDON AF, CARRAT F, MOUTHON L *et al:* Vasodilator drugs and heart-related outcomes in systemic sclerosis: an exploratory analysis. *RMD Open* 2024; 10(4): e004918. https://doi.org/10.1136/rmdopen-2024-004918
9. MALATINO LS, GRASSI R, STANCANELLI B *et al:* Release of immunoreactive endothelin from the heart during percutaneous transluminal coronary angioplasty. *Am Heart J*. 1993;126(3 Pt 1):700-2. https://doi.org/10.1016/0002-8703(93)90421-5