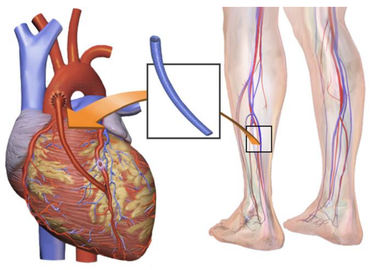
Preclinical validation of VasCraft: A human-derived decellularized and re-endothelialized tissue-engineered vascular graft in a porcine arterial model

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INTRODUCTION

Coronary artery bypass grafting (**CABG**) is a widely used surgical intervention for severe coronary artery disease, aiming to restore myocardial perfusion by bypassing occluded coronary arteries with autologous vessels as a graft.



Autologous grafts used:

- Saphenous Vein.
- Internal Mammary Artery.

Limitations:

- Harvesting-related complications.
- Long-term patency issues.
- Scarcity of suitable vessels.

Researchers have been pursuing **tissue-engineered vascular grafts** for the creation of the optimal, small-diameter (**<6 mm**) **conduit for CABG surgery**, though they have **not yet succeeded**

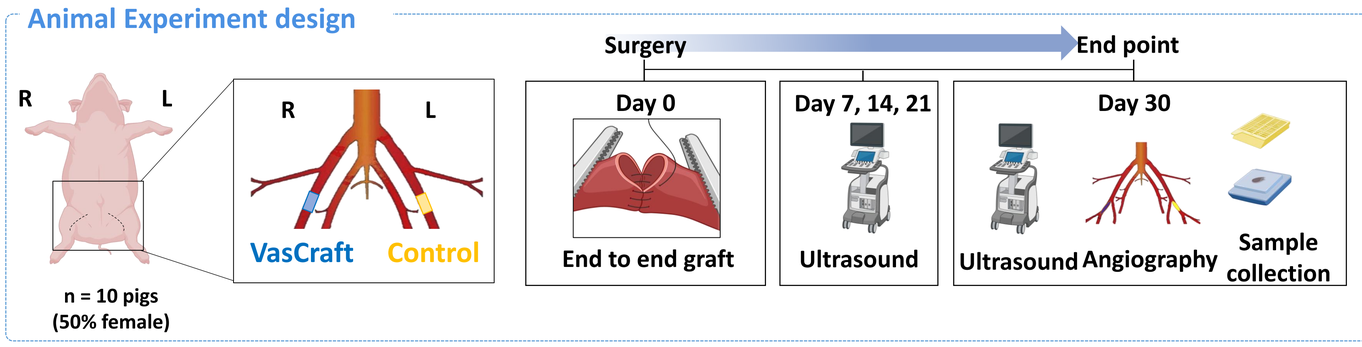
PURPOSE

This study aims to preclinically validate VasCraft, a bioengineered human vascular graft composed of a decellularized human saphenous vein re-endothelialized with umbilical cord blood-derived endothelial cells, as a potential coronary bypass conduit in a translational animal model.

METHODS

Ten Landrace × Large White treated pigs[1,2] (38.9 ± 3.1 kg) were implanted with VasCraft grafts in the right femoral artery and the control graft (the autologous extracted native fragment from the right artery) in the left one.

Animal Experiment design



	In vivo Analysis	*Ex vivo analysis*	*Advanced analysis*
1. Surgical validation	Control graft		—
2. Hemodynamic assessment	Colour Doppler Ultrasound Angiography	Doppler measurements (Vr)	—
3. Wall integrity	—	Histological staining Morphometric analysis	IF (CD31, αSMA, Col I)
4. Biocompatibility	—	Histology (cell infiltration)	IF (CD68, CD3) Single-cell RNAseq

[1]**Immunosuppressive treatment:** Mycophenolate mofetil (500 mg /day); Cyclosporine A (26 mg/kg/day); Abatacept (12.5 mg/kg every 15 days)

[2]**Antiplatelet treatment:** Clopidogrel (150 mg/day); Acetylsalicylic acid (300 mg/day)

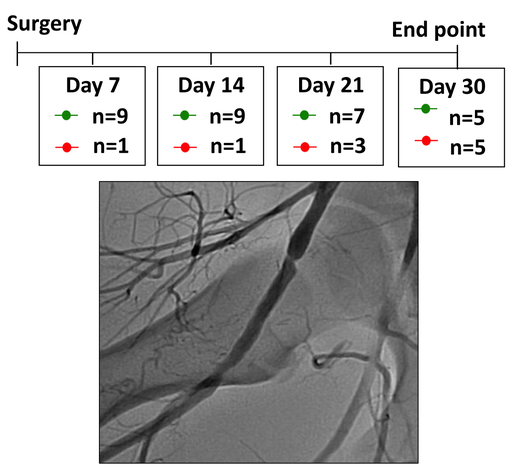
RESULTS

Successful surgical implantation in all animals

Surgical implantation was successfully performed in all animals. Animals recovered uneventfully during the 30-day follow-up. All control grafts remained patent throughout the study period.

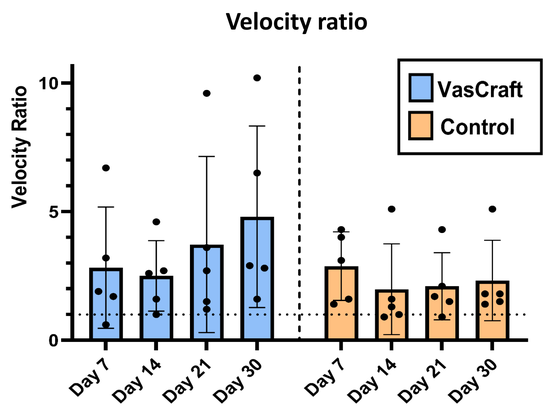
VasCrafts' hemodynamic assessment

50% of VasCraft grafts were patent at day 30; monitored by colour Doppler ultrasound and confirmed by angiography.



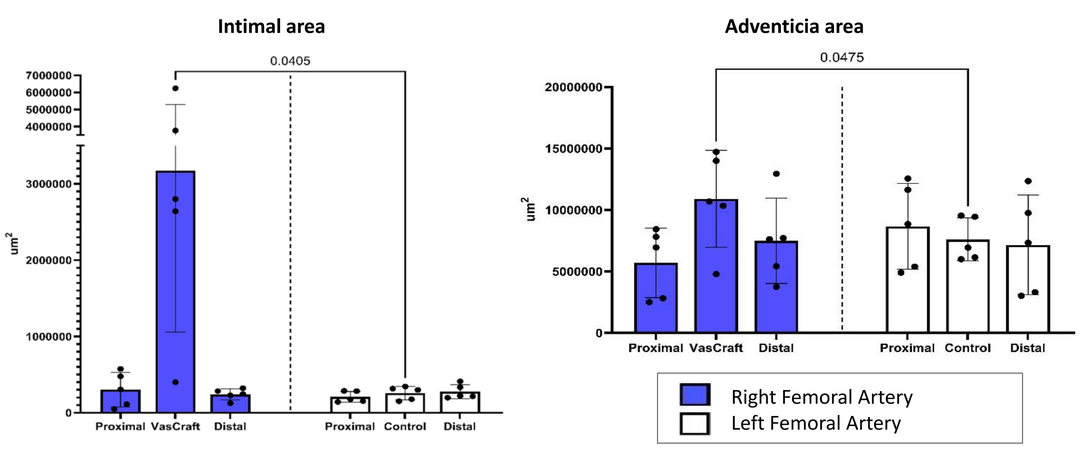
Angiography of patent VasCraft graft on day 30

The velocity ratio (VR) for % stenosis showed no significant differences between control and VasCraft grafts throughout the study.



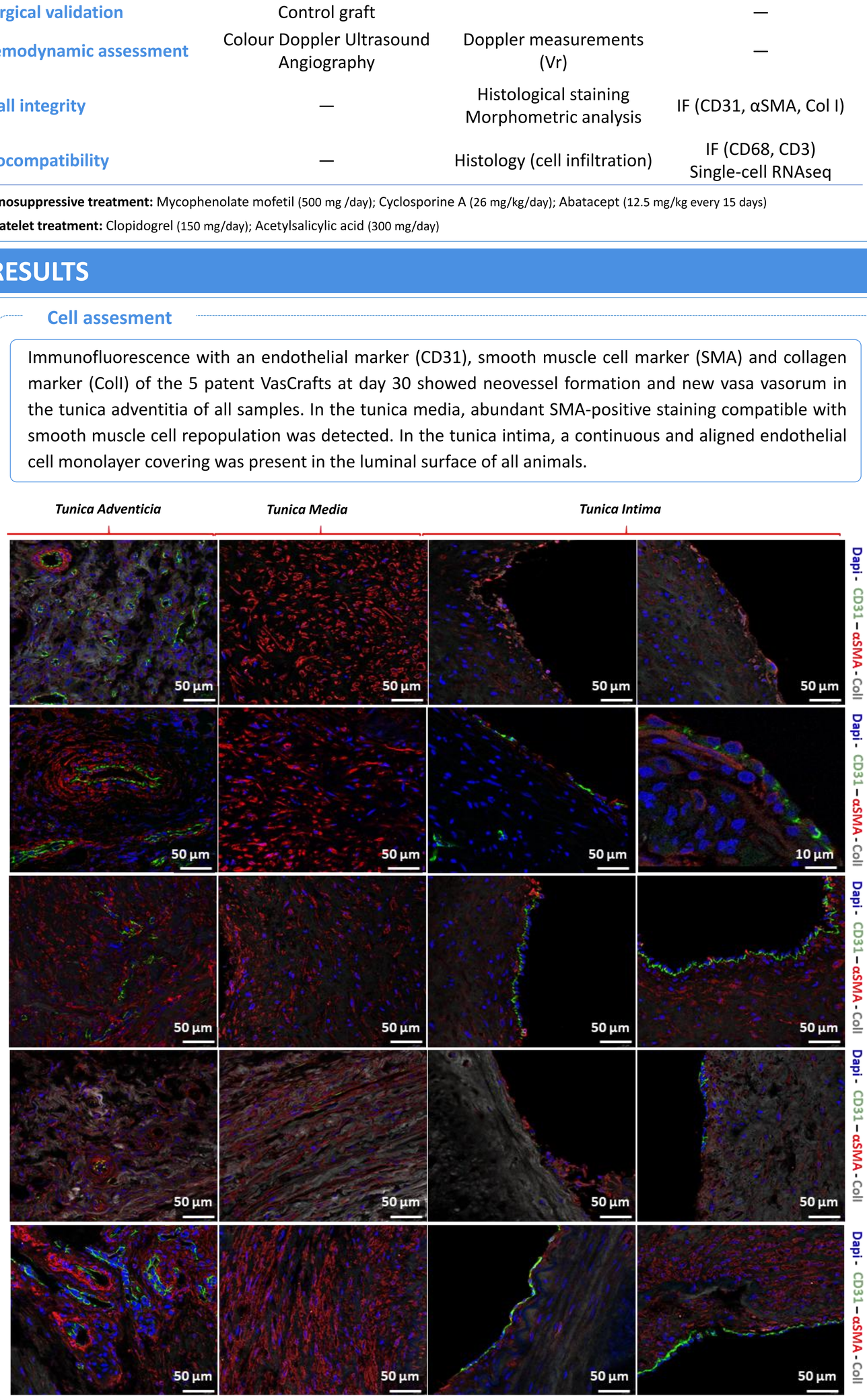
Histological evaluation of graft remodeling

Modified Gallego staining of the 5 patent VasCrafts was performed to quantify structural areas (lumen, intima, media and adventitia). The proximal segment, the graft segment, and the distal segment of the right femoral artery were analysed against its control, the left artery. Results showed an increased VasCrafts' intimal and adventitial area, compatible with early arterialization process and with host–graft integration, respectively.



Cell assesment

Immunofluorescence with an endothelial marker (CD31), smooth muscle cell marker (SMA) and collagen marker (ColI) of the 5 patent VasCrafts at day 30 showed neovessel formation and new vasa vasorum in the tunica adventitia of all samples. In the tunica media, abundant SMA-positive staining compatible with smooth muscle cell repopulation was detected. In the tunica intima, a continuous and aligned endothelial cell monolayer covering was present in the luminal surface of all animals.



CONCLUSIONS

1. VasCraft graft implantation was feasible, with 50% graft patency at 30 days, demonstrating short-term functionality in vivo.
2. Hemodynamic performance was comparable to control grafts in patent samples.
3. Histological and immunofluorescence analyses revealed active vascular remodelling, including endothelial coverage, smooth muscle cell repopulation, and neovessel formation.

NEXT STEPS

- Future studies will focus on single-cell RNA sequencing to better characterize the cellular phenotype of VasCraft grafts in vivo.
- These findings support further large-scale preclinical studies to evaluate durability, long-term patency, and progressive arterial adaptation of the VasCraft graft