SPECIAL TOPIC SESSION: Cardiovascular tissue engineering: Room E **(14:00–15:30)**

Vascular remodelling of synthetic biodegradable scaffolds

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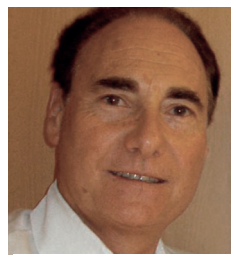

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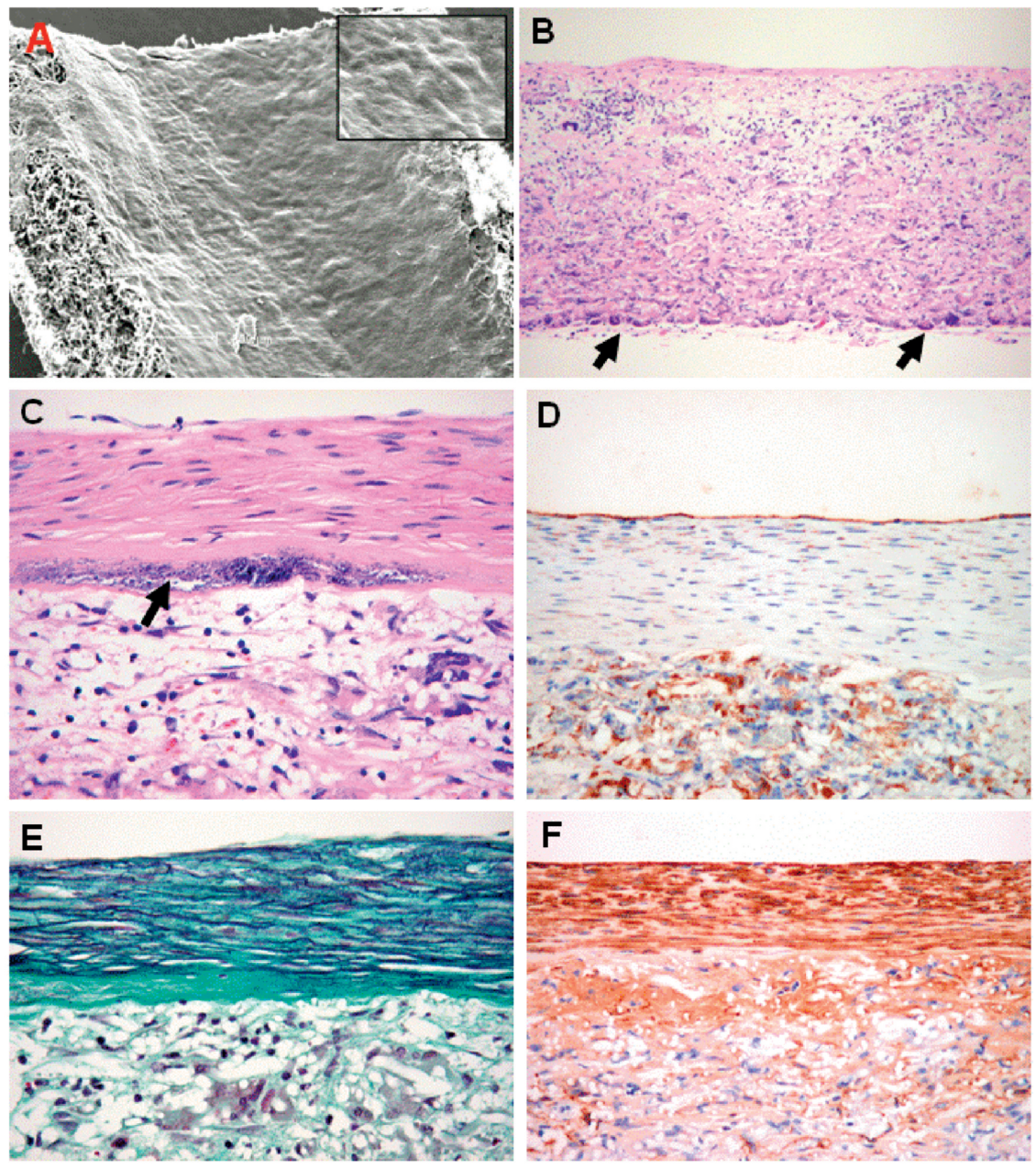
Organ replacement therapy has become one of the main medical activities in elderly patients in the Western world. Estimations raise numbers of 50 Mio patients who have sustained or are supported by an artificial organ or a transplant worldwide. The economic burden is enormous and represents about 10% of the total healthcare spending. Therefore new alternatives have to be investigated in order to repair or replace failing organs such as tissue engineering. Addressing our specialty of vascular tissue engineering as an example, a short outline follows.

Shelf-ready small-caliber grafts are needed for coronary artery and peripheral bypass grafting. Biodegradable scaffolds resistant to aneurysm formation in the systemic arterial circulation have been developed for in vivo vascular tissue engineering. Our long-term study assesses synthetic biodegradable small diameter (2mm) polycaprolactone (PCL)-based vascular grafts compared to ePTFE grafts for aortic replacement in the rat. All grafts were patent with no signs of stenosis, had no aneurysmal dilation despite degradation, were resistant to thrombosis due to confluent endothelialisation, had limited, non-progressing intimal hyperplasia, and had much less calcification than ePTFE grafts. Histologically, a homogeneous cell ingrowth (myofibreblasts and macrophages) produced extra-cellular matrix with collagen and elastin formation with good neoangiogenesis. These grafts may therefore have the potential to provide a better clinical outcome for small vessel revascularization procedures than ePTFE grafts. In the light of this study, a more complete evaluation of the long term healing characteristics of this 'de novo vascular graft' formation must be performed. Thus, such novel in situ tissue-engineered grafts could become a future option for clinical applications such as coronary artery or peripheral bypass grafting.



Morphological analysis of PLC grafts. (A) SEM image of the lumen of the PCL graft after explantation showing complete endothelialization. (B) Longitudinal section of the graft wall showing homogenous cellular infiltration giant cells on the periphery (arrows; HE staining, 100x magnification). (C) Neo-intima with spindle shape cells above a calcified area, indicated by the arrow. An endothelium is present on the luminal side. (HE staining, 200x magnification). (D) Immunohistochemistry anti CD31 labeling endothelial cells on the luminal side (200x magnification) (E) Elastin deposition in the neo-intimal layers is revealed in blue and collagen deposition is revealed in green by a Miller-Masson staining (200x magnification). (F) Immunohistochemistry anti Smooth Muscle Actin demonstrating positivity in spindle shape cells forming the neo-intima (200x magnification).

Preoperative evaluation and optimising patient outcomes II: Room K **(15:50–17:20)**

Iatrogenic hypoglycaemia secondary to tight glucose control is an independent determinant for mortality and cardiac morbidity

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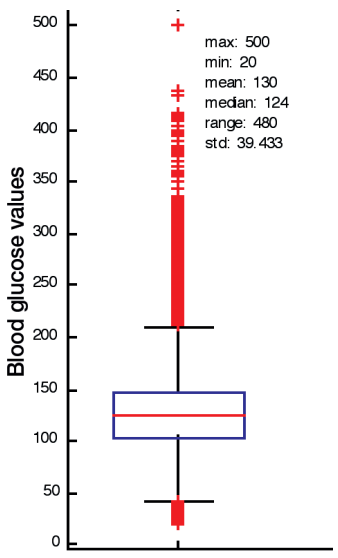
Hyperglycaemia in critically ill patients or in the perioperative phases of major surgical procedures seems to be associated with increased mortality and morbidity. For this reason, many researchers have proposed tight glucose control (TGC) as an effective tool to prevent the deleterious effects of glucose unbalance. There has been considerable recent controversy over the safety of TGC that may lead to iatrogenic hypoglycaemia.

We performed a detailed comprehensive analysis on different glycaemic parameters in a group of patients undergoing TGC after cardiac surgery. Our interest focused, not only on punctual glycaemia values, but also on the impact of other glycaemia data including glycaemia variability, presence and eventual duration of hyperglycaemia (>126 mg/dl), presence and frequency of hypoglycaemia (<70 mg/dl). Insulin drip was used to target ICU glucose levels between 80–126 mg/dl in a consecutive series of adult cardiac surgery patients.



We used univariate and multivariate logistic regression to predict the occurrence of in-hospital morbidity/mortality. The variables analyzed were the comorbidities, the type of surgery, and the temporal glycaemic variables. A total of 596 patients were included and over 8,000 glycaemia measurements were recorded.

From the analysis of the ICU glycaemia data emerged: mean glycaemia 130±39.4 mg/dl (20-500mg/dl), median glycaemia 124 mg/dl, mean standard deviation 31.0, mean hyperglycaemic index (HGI: area under the curve (AUC) for glycaemia>126 mg/dl divided by total length of stay in ICU expressed in hours), 13.7±12.4 (0-91.3), median HGI 10.4.

A total of 123 patients (21%) had at least 1 episode of hypoglycaemia (<70mg/dl) with an average of 2.4 episodes per patient (from 1 to 17 episodes).

Multivariate analysis findings are summarized in the table and remained unchanged after adjusting for age and gender.

Since hypoglycaemia seemed to play an important role in the occurrence of mortality, we identified independent determinants for hypoglycaemia as well. Chronic renal failure (p=0.01; OR=24.9) and diabetes (p=0.0001; OR=22.8) were the sole determinants for ICU hypoglycaemia occurrence.

In the present study, in spite of adequate TGC and achievement of glycaemic targets, hypoglycaemia occurred with a considerable rate.

In our experience, even a single episode of hypoglycaemia seems to impact significantly upon in-hospital mortality (OR=8.3) and the higher is the number of hypoglycemic events, the more significant is the OR for mortality (increasing 1.4 times per every extra episode of hypoglycaemia). We also reported a significant correlation between hypoglycaemia occurrence and requirement for post-operative forms of ventricular mechanical assistance such as extra-corporeal membrane oxygenator (ECMO) and post-operative intra-aortic balloon pump (IABP). These findings suggest a possible relationship between occurrence of low glucose concentration and heart dysfunction.

Interestingly, none of the other blood glucose punctual or temporal trends/variability data, including the markers of very poor blood glucose control (such as glucose standard deviation and HGI), seemed to impact independently upon mortality and major morbidity.

Finally, our findings confirm that diabetes and chronic renal failure are independent determinants for hypoglycaemia.

In conclusion, TGC may result in iatrogenic hypoglycaemia in spite of timely glucose monitoring. Although the morbidity and mortality benefits of TGC have been broadly demonstrated in the past, it is also necessary to evaluate how much the occurrence of hypoglycaemia may mitigate the benefits of TGC.

Furthermore, although the threshold for hypoglycaemia is not well defined, we have clearly demonstrated that even blood glucose levels lower than 70 mg/dl have a strong impact upon mortality and cardiac morbidity after cardiac surgery procedures.

	Obese	Liver Dysf.	COPD	Multi Valve	CRF	Hypogl.	# Hypogl. Episodes	Dialysis	Vent. surgery
Death	OR=11 p=0.01 CI=1.7-71.7	OR=7 p=0.02 CI=1.2-48				OR=8.3 p=0.02 CI=1.2-54.8	OR=1.4 p=0.002 CI=1.1-1.8		
Resp. Failure	OR=4.3 p=0.004 CI=1.5-12.0	OR=4.3 p=0.007 CI=1.4-12.8	OR=4.1 p<0.0004 CI=1.8-9.0				OR=1.3 p=0.03 CI=1.0-1.6		
Tracheo	OR=8.1 p=0.006 CI=1.7-36.9	OR=6.6 p=0.01 CI=1.5-29.2		OR=6.6 p=0.002 CI=1.9-23.1		OR=8.1 p=0.003 CI=2.0-33.2			
CVA				OR=16.2 p<0.0001 CI=4.1-62.6					
Wound Infection	OR=3.6 p=0.03 CI=1.0-12.2								
Post-op Bleeding								OR=9.6 p=0.01 CI=1.6-56.2	
ARF				OR=7.1 p=0.008 CI=1.6-31.4	OR=9.5 p<0.0001 CI=2.8-32.6				
Post-op IABP							OR=1.2 p=0.03 CI=1.0-1.6		OR=18.2 p<0.0001 CI=4.0-81.5
ECMO						OR=9.4 p=0.04 CI=1.0-81.3			OR=18.5 p=0.009 CI=2.0-170.3