IN BRIEF

HEART FAILURE

Device-based fluid system to guide diuretic therapy

Although loop diuretics are essential for the management of congestion in acute heart failure (AHF), an established, evidence-based protocol for optimal diuretic use has not yet been developed. Investigators of the TARGET-1 and TARGET-2 non-randomized, prospective studies now report that the Reprieve system, a device-based fluid management system used to guide diuretic therapy, is safe and effective in regulating fluid loss in the AHF setting. A total of 19 patients (18 men) hospitalized for AHF and showing signs of congestion received diuretics in combination with the Reprieve system for 24 h. The device was designed to measure urine output and to automatically deliver a volume of hydration fluid to maintain the fluid balance rate set by the clinician. With the aid of the Reprieve system, the efficacy end point of preventing excess fluid loss was met by both studies. Furthermore, fluid removal guided by the Reprieve system was safe, well-tolerated and not associated with haemodynamic instability.

ORIGINAL ARTICLE Biegus, J. et al. Controlled decongestion by Reprieve Therapy™ in acute heart failure: the results of the TARGET-1 and TARGET-2 studies. *Eur. J. Heart Fail.* https://doi.org/10.1002/ejhf.1533 (2019)

VALVULAR DISEASE

Incidence of new-onset AF after TAVI and AVR

New-onset atrial fibrillation (AF) is a common complication affecting patients who undergo aortic valve replacement (AVR) and transcatheter aortic valve implantation (TAVI), according to a population-based, observational study. The analysis included 48,715 patients admitted to hospital to receive TAVI and 122,765 to receive AVR. New-onset AF was observed in 50.4% of TAVI hospitalizations and 50.1% of AVR hospitalizations. Patients with new-onset AF also had a greater prevalence of coronary artery disease, congestive heart failure and peripheral vascular disease than those without new-onset AF. Furthermore, new-onset AF was associated with prolonged hospitalization and higher in-hospital mortality.

ORIGINAL ARTICLE Kalra, R. et al. Evaluation of the incidence of new-onset atrial fibrillation after aortic valve replacement. *JAMA Intern. Med.* https://doi.org/10.1001/jamainternmed.2019.0205 (2019)

ATRIAL FIBRILLATION

Nerve cell injury predicts success of AF ablation

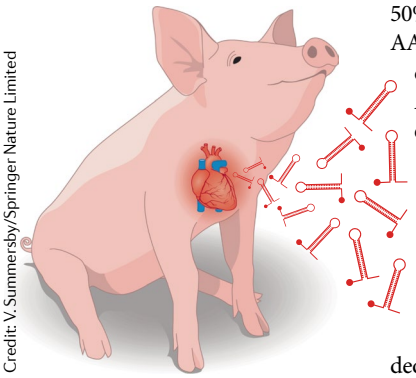
Patients with symptomatic atrial fibrillation (AF) often undergo catheter ablation, during which pulmonary veins are electrically isolated from the atrium. Many key components of the intrinsic cardiac autonomic nervous system (ICNS) are located in close proximity to ablation sites near the pulmonary veins and might be damaged during the procedure. However, the effect of ICNS injury on treatment outcomes is poorly understood. In a study published in *Sci. Transl Med.*, patients who showed greater release of S100B, a neuronal injury marker produced by cardiac glial cells during catheter ablation of AF, were less likely to experience recurrent AF compared with patients who had minimal increases in this neuronal marker. S100B is released upon damage to the ICNS and can induce neurite outgrowth in intracardiac neurons. These findings show that S100B release from glial cells is an indicator of acute intracardiac neural damage during AF. "Further studies should assess the value of targeting the ICNS during ablation and impact on patient outcomes," conclude the investigators.

ORIGINAL ARTICLE Scherschel, K. et al. Cardiac glial cells release neurotrophic S100B upon catheter-based treatment of atrial fibrillation. *Sci. Transl Med.* **11**, eaav7770 (2019)

CARDIAC REGENERATION

MicroRNA-directed cardiac repair after myocardial infarction in pigs

Viral vector delivery of microRNA-199a (miR-199a) after myocardial infarction (MI) in pigs can stimulate endogenous myocardial repair mechanisms and improve cardiac function; however, persistent expression of the miRNA leads to sudden arrhythmic death. "Achieving cardiac repair through the stimulation of endogenous cardiomyocyte proliferation is attainable in large mammals, however dosage of this therapy needs to be tightly controlled," summarize the investigators.



Credit: V. Summersby/Springer Nature Limited

MI was induced in 25 pigs, which were then randomly assigned to receive injections into the left ventricular wall of adeno-associated virus type 6 (AAV6) particles that were either empty or contained miR-199a. An additional group of pigs underwent a sham operation. At 4 weeks after MI, scar mass and size measured by cardiac MRI were approximately 50% smaller in pigs treated with AAV6-miR-199a than in the AAV6-control group. In pigs injected with AAV6-miR-199a, left ventricular ejection fraction recovered after 28 days but in the AAV6-control group, remained >20 percentage points below values in the sham-operated group. Of note, functional improvement in the AAV6-miR-199a group correlated with increased cardiomyocyte dedifferentiation and proliferation.

CARDIAC REGENERATION

Placental stem cells can regenerate the heart

Cells expressing caudal-type homeobox 2 (CDX2) isolated from mouse placentas and administered to mice with myocardial infarction (MI) can selectively home to the heart and differentiate into cardiomyocytes and vascular cells to improve cardiac function, according to a study led by Hina Chaudhry. "We have now uncovered a stem cell that can be isolated from an adult organ, is very primitive and has all the properties of embryonic stem cells but more functions than embryonic stem cells," says Chaudhry.

Chaudhry and colleagues had previously shown that fetal-derived cells can migrate from the placenta to the injured maternal heart. Given that almost 40% of these cells express the homeodomain protein CDX2, the investigators sought to determine whether intravenous delivery of $CDX2^+$ cells can regenerate the infarcted myocardium.

A lineage-tracing strategy was used to label CDX2-expressing cells and their progeny with enhanced green fluorescent protein (eGFP). Placental $CDX2^+eGFP^+$ cells clonally proliferated and differentiated in vitro into spontaneously beating cardiomyocytes that expressed cardiac-specific markers such as troponin T and sarcomeric actinin. $CDX2^+eGFP^+$ cells also differentiated into endothelial-like cells and smooth muscle cells. Importantly, these differentiated cells seemed to have an immunologically naive phenotype, as they had very low expression of most of the major genes related to adaptive and innate immune responses. Placental $CDX2^+$ cells might, therefore, be able to evade the host immune surveillance, a critical feature for allogeneic cell-based therapies.

Finally, the investigators assessed the regenerative potential of placental