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SMART WEARABLE DEVICES IN CARDIOVASCULAR CARE

Technology has increasingly entwined into everyday life and the digital health revolution is upon us. Smart wearables are connected electronic devices that can be worn on the body as an accessory or embedded into clothing. For instance, these include smartwatches, rings, wristbands and skin patches and they all have high processing power and numerous sophisticated sensors that can glean new health insights especially into our cardio-metabolic health. These devices have the potential to challenge the traditional paradigms of prevention, diagnosis and management of chronic cardiovascular risk. Allowing access of wearable-captured data to healthcare providers facilitates remotes patient health monitoring and bridges the physical interaction with patients and the mobility, diverse lifestyles and personalized health targets that defines individualized patient needs. New patient friendly platforms such as Heads Up Health (headsuphealth.com) also increase patient engagement by integrating the myriad of devices that allow easy tracking of numerous cardio-metabolic parameters and the influence of lifestyle (sleep, diet, exercise, stress). This constant stream of data allows clinicians to understand their patient's health more closely and pro-actively adjust management decisions.

Devices have a role to play in the management of cardiovascular risk reduction, the screening, diagnosis and surveillance of common conditions – arrhythmias, heart failure and post procedural care / rehabilitation.

Common statements by patients such as "I run twice each week and do a longer run at the weekend" are too general, subjective and lack important detail such as intensity, sedentary time and absolute energy expenditure. Devices have the capacity to accurately and objectively determine training metrics, which in turn allow proper individualized and target driven daily or weekly goals.

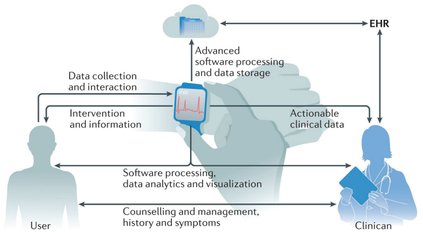
Heart rate (HR) measurements can be used to predict the risk of cardiovascular disease. In healthy populations, a high resting HR has been associated with an increased risk of coronary artery disease and all-cause death and is also well recognized as a predictor of adverse outcomes in patients with heart failure. An impaired HR recovery after exercise correlates with increased adverse cardiovascular events.

Some smartwatches can record a single-lead ECG as needed by pressing a crown (negative electrode) on the side of the watch, with the back of the watch serving as the positive electrode. Single-lead ECGs are useful to diagnose simple and common arrhythmias such as atrial fibrillation (AF). However, they are often insufficient for the accurate diagnosis of more complex arrhythmias. The ongoing HEARTLINE trial is the first randomized trial to investigate whether detecting symptomatic and asymptomatic AF with the use of an Apple Watch improves clinical outcomes. The trial aims to recruit 150,000 US residents aged ≥65 years and evaluate whether AF detection with a wearable device improve AF diagnosis, reduce hard outcomes and increase compliance with anticoagulation therapy.

Blood pressure is leading cause of global morbidity and mortality and the value of remote monitoring is discussed by Dr Macdonald. Future studies are needed to determine whether continuous blood pressure data derived from new generation cuff-less wearables have any clinical significance.
Biochemical sensors can measure body fluid electrolytes with the use of electrochemical transducers, offering valuable information about plasma volume status and analyte concentration. The most common biochemical sensors are the minimally invasive continuous glucose monitors that have been clinically validated but are difficult to embed in consumer-grade wearables and mostly function as stand-alone products.

Drawbacks and several key challenges do remain to embracing smart wearables. Although available evidence supports the use of wearable devices in cardiovascular disease prevention, diagnosis and management, large, well-designed trials are needed to establish their advantages. There is a valid concern for device accuracy, protecting patient privacy and cost, and how to separate actionable data from noise.

The figure shows how wearables can be optimally integrated in patient care. Wearable data can provide immediately actionable clinical metrics to health care providers. The data can be harnessed to provide personalized, real-time and adaptive interventions delivered directly to the patient. Finally, the wearable data can be continuously stored in secure, personal health clouds or electronic health records (EHR) for advanced data processing and sharing with third parties through transparent data user agreements.



Conclusion
The march of smart wearables is relentless and it's now a question of not if but how they evolve to disrupt and hybridize with clinic -based models of care delivery. A legacy of the Covid-19 pandemic may well be to accelerate the integration of smart wearables into cardiovascular care for the benefit of patients.

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REMOTE MONITORING TO CONTROL BLOOD PRESSURE

Hypertension affects about 30% of adults in Singapore, and is one of the most common conditions that present to primary care. Usual care for hypertension is based around 3-6 monthly visits. At the patient visit, a BP reading will be taken (or sometimes the patient will have recorded some data at home). This single data point will then be used to assess control and determine if any lifestyle or medication changes are necessary. There is now substantial evidence that these one-off readings do not accurately represent a patient's overall control. Leaving patients with poorly controlled blood pressure and an increased risk of cardiovascular events.

New evidence from the STEP trial has added to the weight of literature encouraging tighter BP control to reduce cardiovascular events. The STEP trial enrolled 9624 Chinese patients with hypertension aged 60-80 years. Patients were randomized to targets of < 110mmHg or <130mmHg. At 1 year of follow up the mean BP in the tight control group was 127.5mmHg and in the less tight group was 135.3mmHg. Over a median follow-up of 3.34 years, the tight control group had a significantly lower rate of strokes, heart attacks, heart failure, and CV death.

Data like this highlights the benefits of tighter control. However, the current care model does not lend itself to achieving these targets. Remote monitoring of hypertension may be the key. hypertension is an excellent disease to track remotely. It can be measured non-invasively. There is the wide availability of blood pressure monitors and they are relatively low cost. It is a disease that is measured in numbers so clear targets can be set for treatment. There have now been numerous studies and systematic reviews that have demonstrated the benefits of telemonitoring for the treatment of hypertension.

One clinical trial performed in primary care randomized 450 patients with uncontrolled hypertension to home BP telemonitoring with pharmacist intervention versus usual care. Patients were given 2 weekly calls with a pharmacist until BP was stable and on target and then this was reduced to monthly calls until 12 months was completed. The telemonitoring arm was associated with significantly better blood pressure lowering at 6 and 12 months at -10.7mmHg and -9.7mmHg respectively when compared to usual care.

This was sustained even after the intervention ended; at 18 months the difference between the arms was still -6.6mmHg. (*JAMA Network Open*. 2018;1(5):e181617)

The correct structure of a remote monitoring program for hypertension is important. Although patients can monitor their blood pressure at home, the problem comes in them knowing what to do with the information, this is when a remote monitoring service really becomes valuable. If you have a member of the healthcare team checking the data and providing actionable feedback to the patient, then BP control can be improved. The ideal telemedicine program for hypertension should include remote monitoring of vital signs; education on lifestyle and risks; message or video consultations with a member of the healthcare team to allow drug titration.

If properly implemented, there are a multitude of benefits to digital monitoring in hypertension:

- Less frequent visits
- Patient engagement in their health
- Improved QoL
- Improved medication adherence
- Catch side effects early before they become an issue
- Reduction in care costs

Large healthcare systems like the NHS in the UK are already piloting remote monitoring programs for hypertension. This new approach to care will likely become the standard of care within the next 10 years, with measurable benefits to both the individual and society.

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EXPANDING INDICATIONS FOR SGLT-2 INHIBITORS BEYOND DIABETIC CONTROL

Overview:
Sodium-glucose co-transporter 2 (SGLT-2) inhibitors are a relatively new class of antidiabetic agents that improve glycaemic control by blocking glucose reabsorption at the proximal renal tubule thereby increasing urinary glucose excretion. It is becoming increasingly clear that SGLT-2 inhibitors also have important beneficial actions on the cardiovascular (CV) system over and above their effect as diabetic drugs. Figure 1 summarizes some of the CV benefits of SGLT-2 inhibitors in the kidneys, vasculature, adipose tissue, liver, pancreas and heart.

Landmark clinical trials:
In recent years, a number of landmark CV outcome trials (CVOT) have shown that SGLT-2 inhibitors reduce the rates of CV events as well as the risk of the composite outcome of CV death or hospitalization for heart failure. [1-3] The first major study in this field was the EMPA-REG OUTCOME trial (Empagliflozin, CV Outcomes, and Mortality in Type 2 Diabetes) published in 2015 [1]. The study was conducted among patients (≥ 18 years) with T2DM at high risk for CV events. A total of 7,020 patients were randomized to a daily dose of empagliflozin 10 mg (n = 2,345), 25 mg (n = 2,342) or placebo (n = 2,333). The primary outcome was a composite of CV death, nonfatal MI (excluding silent MI), or nonfatal strokes. The empagliflozin group had a significant reduction in the primary outcome compared to the placebo group (10.5% vs. 12.1%, HR: 0.86, 95% CI: 0.74 - 0.99; P = 0.04 for superiority and P < 0.001 for non-inferiority). The CVOT for dapagliflozin (Dapagliflozin Effect on CV Events–Thrombolysis in Myocardial Infarction 58, DECLARE-TIMI 58) demonstrated its CV safety and benefit in reducing the risk of hospitalization for heart failure and the occurrence of renal adverse events in patients with T2DM and high CV risk. [3] The trial randomized 17,160 patients to a daily dose of dapagliflozin 10 mg daily (n = 8,852) or placebo (n = 8,578). Dapagliflozin met the non-inferiority criteria; however, it did not result in a lower rate of major adverse CV events compared to placebo (8.8% vs. 9.4% events/1,000 patient-years, HR: 0.93, 95% CI: 0.84 - 1.03; P = 0.17). But for efficacy, dapagliflozin lowered the rates of CV death or HF hospitalization compared to placebo (4.9% vs. 5.8%). Treatment with dapagliflozin was associated with a clinically meaningful reduction in the rate of renal events. The cardiorenal secondary composite of ≥ 40% decrease in eGFR to < 60 mL/min/1.73 m2, new end-stage renal disease or death from renal or CV cause occurred less often in patients treated with dapagliflozin (370 patients out of a total of 8,582) than in the placebo group (480 patients out of a total of 8578) (HR 0.76; 95% CI 0.67 to 0.87). As a result, dapagliflozin was given regulatory approval to treat adults with chronic kidney disease without diabetes in the European Union in August 2021. It was the first SGLT-2 inhibitor to receive this designation in Europe.

Benefits in patients with heart failure:
SGLT-2 inhibitors have also been shown to confer CV benefits in patients with heart failure even in patients without diabetes. DAPA-HF was conducted in patients with heart failure with reduced ejection fraction (HFrEF) to evaluate the effect of a daily dose of dapagliflozin 10 mg in comparison to placebo, in addition to standard care [4]. The study randomized 4,744 HFrEF patients and an eGFR ≥ 30 mL/min/1.73 m2 to dapagliflozin 10 mg daily (n = 2,373) or a placebo (n = 2,371), irrespective of T2DM status for 18.2 months follow-up. The mean age was 66 years, 24% were females and 42% were diabetic. The trial showed that dapagliflozin lowered the risk of death and HF hospitalization in patients with HFrEF, compared to placebo, regardless of the presence or absence of diabetes. Similarly, the EMPEROR-REDUCED trial investigated the impact of empagliflozin on hospitalization in patients with HFrEF with or without diabetes [5]. The study randomized 3,730 patients with class II, III, or IV HFrEF to a daily dose of empagliflozin 10 mg or placebo. The primary outcome (CV death or HF hospitalization) was significantly less in the empagliflozin group (19.4% vs. 24.7% with P value < 0.001). Secondary outcomes consisted of total number of HF hospitalization, which was also significantly lower in the empagliflozin group (388 events vs. 553 events). Also, the rate of eGFR decline was significantly lower in the empagliflozin group during the study time. As a result of these two recent landmark studies showing benefits of SGLT-2 inhibitors in patients with HFrEF, the European Society of Cardiology Guidelines has been updated this year to give dapagliflozin and empagliflozin a class 1 indication in reducing the risk of heart failure hospitalization and death in patients with HFrEF [6].

So far, no effective treatment has been shown to improve the morbidity and mortality in patients with heart failure with preserved ejection fraction (HFpEF), but there are ongoing trials with SGLT-2 inhibitors in this field with some promising initial results.

Conclusion: Based on the results of major landmark clinical trials, SGLT-2 inhibitors have not only shown substantial CV benefits (reduction in the risk of HFrEF hospitalizations or composite CV deaths), but also reduction of kidney diseases. This class of medication should therefore no longer be seen as add-on drugs to improve glycaemic control but rather as an important therapy in their own right for treating patients with high CV risk profiles, regardless of their diabetic status.

SUMMARY POINTS:

- *SGLT-2 inhibitors significantly reduce the risk of major CV events, CV death or hospitalization for heart failure and progression of chronic kidney disease in people with type 2 diabetes mellitus (T2DM) with or without atherosclerotic cardiovascular disease.*
- *Dapagliflozin and empagliflozin have shown significant beneficial effects on the composite outcome of worsening of heart failure or CV death in patients with NYHA Class 2, 3 or 4 heart failure with or without T2DM.*
- *Dapagliflozin and empagliflozin significantly reduce hospitalization for heart failure, and dapagliflozin significantly reduces cardiovascular death irrespective of T2DM status.*
- *Dapagliflozin and empagliflozin have significant beneficial effects on renal outcomes in people with and without T2DM.*

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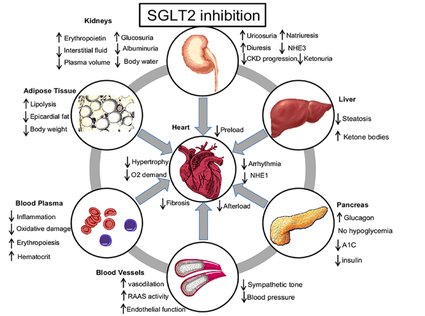
Figure 1. Cardiovascular and renal benefits of SGLT-2 inhibitors



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REMOTE MONITORING FOR THE DIABETIC FOOT IN A PANDEMIC

With the isolation caused by the pandemic, remote monitoring for patients with diabetes is more critical than ever to get information on patients' risk of limb loss from ischemia and ulceration.

Most of us are familiar with devices worn by people every day such as Fitbit telling us our heart rate and how many steps taken throughout the day. Patients can even buy an "ECG" device on Amazon with the tracing they can send to the doctor. Health care is gearing up for remote patient monitoring (RPM) and with our current isolation measures during COVID-19, more devices and artificial intelligence software and hardware that help physicians provide care and monitor their patients more closely, but from a distance, are becoming available.

Remote or wearable patient monitoring devices may be defined as devices that must measure or detect common physiological parameters and must wirelessly transmit patient information to their health care provider or a monitoring entity. New devices on the market need to be HSA approved and the RPM must be monitoring a physiologic factor. We have seen these in medicine, such as the glucometers that patients wear externally so they longer need to prick their fingers and take a reading; blood sugar can now be monitored 24/7. Devices include blood pressure cuffs or wrist bands worn all day long and pulse oximeters and even pacemakers/defibrillators that can send information to alert the doctor if there is a pivotal event.

These are however, but a few remote monitoring devices for diabetic feet. Here we look at a few exciting devices soon to be available at the Harley Street Heart and Vascular Centre.

The Orpyx SI insole (Orpyx Medical Technologies, Figure 1) measures temperature changes continuously and can alert the wearer on their smart phone of the subtle differences in temperature. This would warn patients with diabetes that they may be developing an ulcer. While there are other similar devices like the one from Orpyx, this device monitors both temperature and pressure. The clinical trial completed by Orpyx shows that by wearing the insole even for half the walking hours, ulceration occurrence is significantly reduced.1 However one potential problem with the Orpyx device is that insoles will need to be moved from shoe to shoe if the patient wears more than one pair of shoes, which is highly likely. Adherence with this monitoring program may also be more difficult as the device has to be recharged every night.

Figure 1. The Orpyx SI Diabetic insoles

Siren Socks (Siren technologies, Figure 2) measure foot temperature in real time and again, like the insole that measures foot temperature changes, can assist in alerting the doctor through a dashboard that the physician's office would monitor. When alerted, the doctor would contact the patient to educate him or her to reduce the amount of weight-bearing and shearing that may be causing increased skin temperature in the foot, or to cool the foot to reduce tissue damage. One can see patients wearing this device daily, as most of us wear socks with our shoes on a daily basis. The Siren socks can assist in reduction of friction and shearing, and thus socks with sensors to look at skin temperature changes may be more readily accepted by patients. Both devices meet the goal of offloading the diabetic foot in keeping with the recommendations by the International Working Group for the Diabetic Foot Guidelines for offloading.[2]

Figure 2. The Siren Socks

A 2007 Diabetes Care study discusses the use of an instant total contact cast (TCC).3 It has been instilled in us as wound care providers that offloading the plantar foot ulcer for a patient with diabetes is the gold standard. There is more research showing that a removable cast walker (either made nonremovable or applied to a cooperative patient) can benefit almost equally as having a TCC applied.

Motus Smart (Sensoria Tech, Figure 3) cast walker boots are an exciting new RPM technology for offloading the diabetic foot ulcer or Charcot's foot. There is a rocker plate that can be removed so patients can keep the boot on, and sleep with it on. The boot can be locked so the patient cannot remove it, and it can be adjusted to fit for swelling in legs. Of more interest is that an inner sole with sensors can measure the pressure in the boot from the foot when you fit the patient with it, and it provides continuous monitoring of the patient's level of activity.

Figure 3. Motus Smart cast walker boots for offloading diabetic feet

The pandemic, the additional risks to diabetics and the elderly as well as the restrictions on social interactions imposed by COVID mean that we may need to develop new ways of monitoring chronic disease. Diabetic foot monitoring in particular is a key potential target condition for this, given the relatively high prevalence of this in Singapore and the consequences of limb loss, morbidity and mortality from the failure of a community monitoring for diabetic feet at risk.

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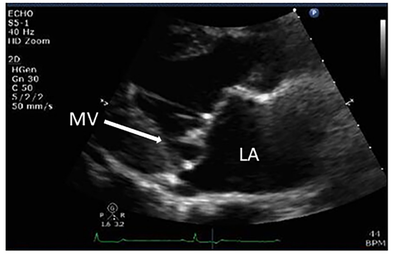
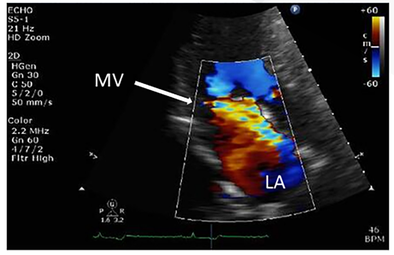
QUIZ





A 50-year-old man who is usually fit and well and cycles 100km every week presented with increasing fatigue and breathlessness over a few weeks. He has no history of cardiovascular disease or any traditional risk factors. Auscultation revealed a pan-systolic murmur in his left sternal region. There were no signs of heart failure and his ECG and baseline blood tests were normal. The echo images are shown in the figure above (parasternal long axis view- MV= mitral valve, LA- left atrium).

Questions:
1) What are the main findings on the echo images?
2) What additional tests would be useful?
3) How would you manage this patient?

Answer is available on our website:
http://www.harleystreet.sg/quiz - answers/medbulletin-Nov-2021/

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THE HARLEY STREET
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INTRODUCTION

The last 18 months have been practice-changing for all of us. COVID-19 has required doctors to examine how we deliver care and has dramatically accelerated the development and adoption of digital medicine across the world. Prior to COVID-19, telemedicine had barely penetrated the market, and now we perform telehealth calls on a regular basis. When the global pandemic starts to abate, this revolution in digital health will be here to stay. In this issue, Dr. Khurana and Dr. MacDonald explore two key areas of the new digital health revolution and how they can be implemented for our patients.

COVID-19 did not appear to slow the progress in clinical trial data in the cardiovascular space. There have been multiple new clinical trials that have changed the way that we manage these patients to optimize their clinical outcomes. Dr. Liew will discuss the key updates in the use of SGLT2 inhibitors; a class of drugs with continually expanding indications. In line with this, Dr. Narayanan will examine the latest advice regarding screening and management of the diabetic foot. We hope you enjoy these articles. If you have any questions or queries we are always available to discuss things by phone or email, and we hope to meet you all in person when rules relax!

From The Harley Street Heart and Vascular Centre

From left to right:
Dr. Sriram Narayanan, Dr. Reginald Liew
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