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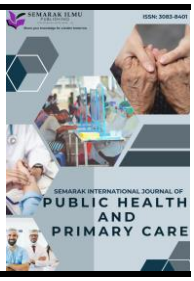

Preparation, Steps, Optimisation, and Troubleshooting the External Counterpulsation (ECP) Device in Regenerative Cardiology - A Clinical Protocol

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ABSTRACT

Heart-related deaths persist worldwide at high rates. As if adding fuel to fire, the global burden, the cost of cardiovascular disease events and its treatment have been climbing steadily with time. As both coronary artery disease and heart failure linger among the costliest ailments to treat, salutary options are direly needed. The external counterpulsation (ECP) is a thoroughly underrated, non-invasive biomedical device. It augments the diastolic phase of the cardiac cycle, increases both venous return and cardiac output, and causes arterial shear injury resulting in numerous supraphysiological benefits. The ECP has been widely utilised across the globe in both therapy and research. However, presently there is no protocol paper on this regenerative cardiology device. In this manuscript, we narrate the protocol that covers the preparation, steps, optimisation, and troubleshooting of the ECP. We believe this device should only be handled by qualified individuals since it requires a foundational understanding of medical physics, biomedical engineering, emergency medicine, internal medicine, cardiology, and regenerative medicine to address a variety of potential problems. We also discuss the legislation of the ECP device and the need for regulation. Finally, it is envisaged that this paper will serve as a model for developing future ECP procedures that are condition- and disease-specific.

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1. Introduction

Heart-related deaths remain the leading cause of mortality in both developed and developing countries [1,2]. The burden of cardiac therapy has also risen over the years. Coronary artery disease (CAD) and heart failure (HF) remain as one of the costliest diseases to treat worldwide [3]. It is estimated that around 17 million would succumb to cardiovascular diseases (CVDs) while 325 million would suffer from disability-adjusted life years by 2029 [4]. Globally, the prevalence of HF is around 9 per 1000 persons [5]. Although the prevalence of HF has decreased in the past decade with conventional cardiology and cardiothoracic surgical advancements, the mortality and hospitalisation remain high[6]. On that account, there is a dire need to make cardiovascular interventions both scalable and affordable to all countries [7–19].

One of the most underrated cardiovascular devices intended for therapy is the external counter pulsation (ECP) device. The current ECP was invented in 1983. Earlier non-invasive works where water bags, pumps and trousers of aviator G-suits were made use of, have been described thoroughly elsewhere by Sorof and Giron [20]. The principles of ECP are an evolution from the invasive intra-aortic balloon pump (IABP) [21]. The ECP is non-invasive and consists of three basic components which are the pneumatic cuffs, air compressor, and an operating computer [22]. The ECP has undergone many facelifts over the years. The principal work of ECP has evolved from manipulating hydraulics to other mechanical pneumatic methods such as air [23,24]. The ECP pneumatic cuffs are rapidly and sequentially triggered by detection of the R wave in the electrocardiogram (ECG) [25]. The monitoring of the counterpulsation is done with a finger photoplethysmogram (PPG) [9,26]. However, the biomedical goal in patients remains the same which is to augment the diastolic phase sufficiently to cause retrograde arterial blood flow, increase venous return, increase cardiac output, and to allow beneficial arterial shear injury.

The counterpulsation causes central and peripheral consequences [27]. Centrally, the ECP causes diastolic augmentation, systolic unloading, and increased venous return. In contrast, peripherally, it causes increased shear stress and effects on endothelial derived substances [27,28]. There is also increased coronary blood flow during counterpulsation [29]. In addition, the continuous effects of shear stress and microinjuries remodel the coronary arteries resulting in collateral circulation. The collateral circulation is a dynamic set of structures which have important consequence for heart protection [30]. Furthermore, this phenomenon is amplified with the increased concentration of vascular endothelial growth factor (VEGF) in the arteries from shear stress [31,32]. The promotion of collateral circulation ameliorates left ventricular dysfunction, reduces infarct size, and decreases mortality [33].

Additionally, ECP is also considered “passive exercise” which causes peripheral conditioning that exerts clinical benefits [27]. ECP improves functional classification in HF [34]. The reduction of aortic pressure and myocardial oxygen demand are some of the parameters responsible for the improvement [34]. Otherwise, the ECP reduces both the preload and afterload by lowering the end diastolic pressure and total peripheral resistance [29,35]. Other clinical benefits of ECP have been extensively discussed elsewhere [36]. Other than that, ECP causes vasodilatation, increase in plasma and platelet cyclic guanosine monophosphate (cGMP), increase in fractional flow reserve (FFR), cluster of differentiation (CD)34+ and CD133+ [27,37].

Although ECP has been widely used in clinical medicine and research, to our best knowledge, there is no ECP protocol paper available. The aim of this protocol paper is to consolidate information by clinicians, scientist, and experienced ECP device operators in a published and peer-reviewed manuscript to narrow the research gap. With this, the current and latest sciences could be

apprehended, compared, and debated with our experiences and expertise. It is hoped that this protocol would be beneficial for the enhancement of patients' safety, maximise the efficacy of the treatment, and improve the outcome of those undergoing ECP. In addition, this protocol could be benchmarked in future ECP related clinical research.

2. Protocol

The protocol was modified from previous ECP textbooks and previous expert consensus [36,38,39]. In addition, most of the authors of this manuscript are active ECP provider and researchers who have safely conducted ECP for several years. As this is a protocol paper, no sample size calculation nor statistical were needed.

The ECP protocol is divided into three phases which include: A) before deciding and implementing the ECP, B) ECP implementation, and C) post ECP implementation.

2.1 Before Deciding and Implementing the ECP

Prior to deciding and implementing the ECP, the patients are subjected to strict consideration of the indication and contraindication criteria. Traditionally, the indication for ECP include refractory cardiogenic shock, and CAD not amenable to percutaneous catheter insertion (PCI) or coronary artery bypass graft (CABG) surgery [28,40,41]. On the other hand, the contraindication for ECP include active deep vein thrombosis (DVT) and other leg swelling that is still being investigated, patients with suspected brain, thorax or abdominal aneurysm(s), aortic regurgitation and stenosis, arrhythmias, pregnancy, active cancer, and lower limb fractures that may be affected by the compression of the ECP cuffs. In addition, special precautions maybe needed for those with arterial or venous catheters, those who have had recent vascular surgeries including arterio-venous fistula (AVF) and those who have hip or lumbar issues. Otherwise, ECP has been proven to benefit non-heart cases such as insomnia and stroke rehabilitation to name a few [31,42–46]. Special precaution should be taken for certain types of HF. Modifications may be needed on cuff size and pressure of the ECP. These have been discussed extensively elsewhere [24]. The indication and contraindication of ECP are depicted in Figure 1.

Indication	
Heart	**Non-Heart**
• Refractory Angina • MI not amenable PCI nor CABG • Heart failure • Cardiogenic Shock • Peri cardiac surgery • No further revascularisation option • Disabling angina • Evidence of inducible ischemia	• Insomnia • Acute hearing loss • TIA and stroke • Erectile dysfunction • Recovery after sports • Metabolic Syndrome • Inflammation and endothelial dysfunction • Lung fibrosis • Post COVID-19 sequelae with lung manifestation • Increase renal function
Contraindication	
Relative	**Absolute**
• Tachyarrhythmia • Hip pain • Lower leg swelling under investigation • Uncorrected coagulopathy • Lower limb wounds • Recent vascular surgery • Aortic stenosis • Aortic insufficiency • Unable to lie flat or in a reclined position • Decompensated HF • Moderate to severe pulmonary hypertension (mean pulmonary artery pressure > 50 mmHg)	• Bradycardia • Brain, thoracic and/or abdominal aneurysm • Sepsis • Deep vein thrombosis • Lower limb fractures • Pregnancy • Severe lower extremity vaso-occlusive disease • Anticoagulant usage with requirement of INR > 2.5 • Aortic regurgitation

Fig. 1. Indications and Contraindications of ECP. *(Abbreviations: CABG: Coronary Artery Bypass Graft, COVID-19: coronavirus disease, DVT: Deep Vein Thrombosis, HF: Heart Failure, MI: Myocardial Infract, PCI: Percutaneous Coronary Intervention, TIA: Transient Ischemic Attack)*

Patients should also be assessed and evaluated via questionnaires, scoring systems, physical examination, and auxiliary workups. The questionnaires that are recommended include Quality of Life and Functional Capacity Scoring, Seattle Angina Questionnaire (SAQ), Rand Short Form 36 Survey Score (SF-36), and Duke Activity Score Index (DASI) [40,44,47]. The New York Heart Association (NYHA) class should also be obtained. A full physical examination could reveal murmurs, presence of abdominal aortic aneurysm (AAA), and the suitability for the patient to lie flat and reclined, as well as the options of using two or three cuffs during the ECP procedure. The ankle brachial systolic index (ABSI) could be considered in some cases. An ECG and transthoracic echocardiogram should be done to evaluate arrhythmias, ejection fraction, valvular disorders, and other anatomical anomalies that may be harmful upon counterpulsation. An ultrasound abdomen could be done in suspected AAA cases as a more specific assessment of the aorta. Ideal blood workups include platelet levels, C-Reactive Proteins, (CRP), Glycated Haemoglobin A1c (HbA1c), and estimated Glomerular Filtration Rate (eGFR). Coagulation profile should be done for those on blood thinners and suspected coagulopathy. Additionally, a 6-Minutes Walking Test (6MWT) and/or nuclear imaging of the heart could be done in facilities equipped with such services [48,49].

Importantly, the ECP procedure should be delayed until certain conditions and illnesses that may get worse with ECP are corrected. These include lower limb wounds with hypoalbuminemia, sepsis, and coagulopathies.

The clinician should also review all the medications and nutraceuticals that are consumed by the patient and adjust or optimise them accordingly prior to ECP. An internal medicine physician, cardiologist and an/or cardiothoracic surgeon consultation may be needed in complex cases, medication optimisation, structural variation and/or anomalies of the heart and vessels, as well as cases with a record of previous heart surgeries. Referral for advanced cardiometry such as stress test and Holter should be conducted when indicated. Additionally, patients with pacemakers and cardioverter defibrillators may need to see a cardiologist and have their device settings adjusted or optimised prior to commencing with ECP [39].

2.2 ECP Implementation

The implementation of ECP could be further divided into pre-procedure, during procedure and post procedure.

2.2.1 Pre-procedure

i. Make sure the patient arrives at least 10 minutes prior to the procedure.
ii. It is recommended to obtain informed consent from the patient at every session prior to the procedure.
iii. Ensure that the ECP room is well ventilated, conducive, and has access to emergency calls and transportation.
iv. Drugs such as oral nitroglycerin, aspirin, intravenous loop diuretics (such as frusemide), and adrenaline should also be readily available in case of anticipated emergencies.
v. An oxygen tank or supply should be within reach during an emergency.
vi. A trained paramedic or medic should be on standby to anticipate any emergencies [48].
vii. Patients may consume their medications, accordingly, as reviewed in the previous part of this manuscript. Any new medication and nutraceutical usage should be informed and discussed with the clinician in charge, as some may affect the rhythm and other related physiological processes of the heart.
viii. Blood thinners should be optimised to reduce the risk of bruising and bleeding during the ECP.
ix. Patients should be asked to empty their bladders prior to the procedure.
x. Blood pressure (BP) is to be taken prior to the procedure. ABSI may be indicated for certain cases.
xi. A weight log should be done prior to each treatment.
xii. A log of wounds at the lower limbs and cuff attachment sites should be recorded and informed to the clinician in charge for evaluation of suitability for the ECP treatment.
xiii. The lungs should be auscultated for any signs of bronchospasm or pulmonary oedema.
xiv. Patients who have “relative” contraindications to ECP should be closely monitored.
xv. Additionally, the operator should ensure that the machine's emergency stop button is always functional.
xvi. The ECP should only be commenced when a clinician has assessed the patient and determined that they are a good fit for ECP. All of these are depicted in Figure 2.

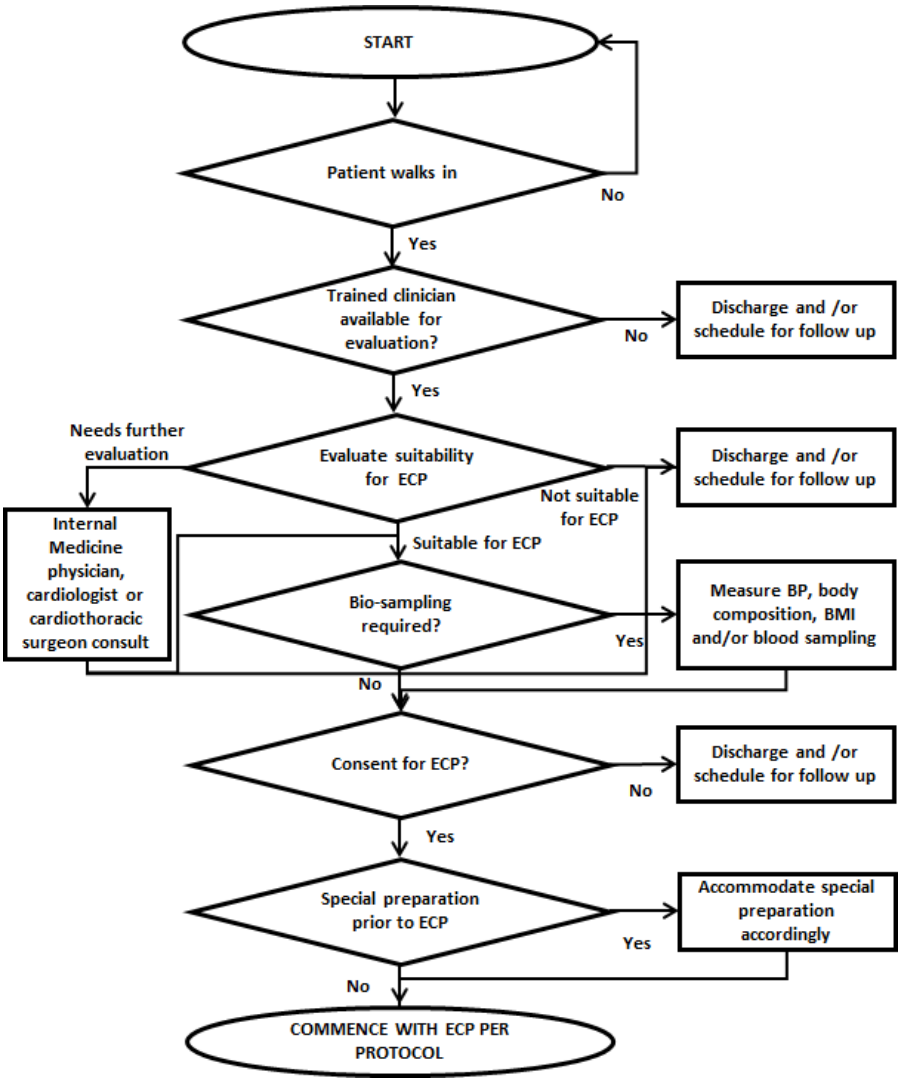

Fig. 2. The proposed workflow prior to commending the ECP

xvii. Unwell patients, those who are unable to lie flat or to the reclination of the bed and have an active leg infection or DVT, should be re-evaluated by a clinician and rescheduled. A modified Well's criteria could be easily scored in the clinical setting after evaluation of unilateral non-pitting oedema of the lower limb[50]. Additionally, calf swelling of more than 3 cm compared to the contralateral side (measured 10 cm below the tuberous tuberosity) can be easily noticed clinically [50,51].

xviii. Patients should wear comfortable pants with a length that covers their ankles.

xix. Any knee braces that interfere with leg and thigh cuff placement should be removed. If the knee brace must be kept, the ECP session should be rescheduled or modified accordingly.

xx. Ensure the placement of the thighs and buttocks cuffs, which passes through the inguinal region, does not impinge on the scrotum. It is advisable for the patient to check this prior to ECP commencement.

xxi. Ideally, the cuff should be placed at the belly of the muscles and adjusted accordingly to obtain the best contraction effect while minimising patient discomfort.

xxii. The operator may opt not to strap the groin belt cuff if a 'two-step' counterpulsation is intended, as depicted in Figure 3. This could be carried out by not strapping certain cuffs

such as the buttocks cuff or by turning off the option on the device control panel as depicted in B) and C) of Figure 3. Specific cuffs could also "opted out" for personalised treatment in clinical conditions such as below knee amputation(s), and back pain.

xxiii. The leg strap is applied at the belly of the calf muscle, thigh muscle and buttocks as depicted in A) of Figure 3.

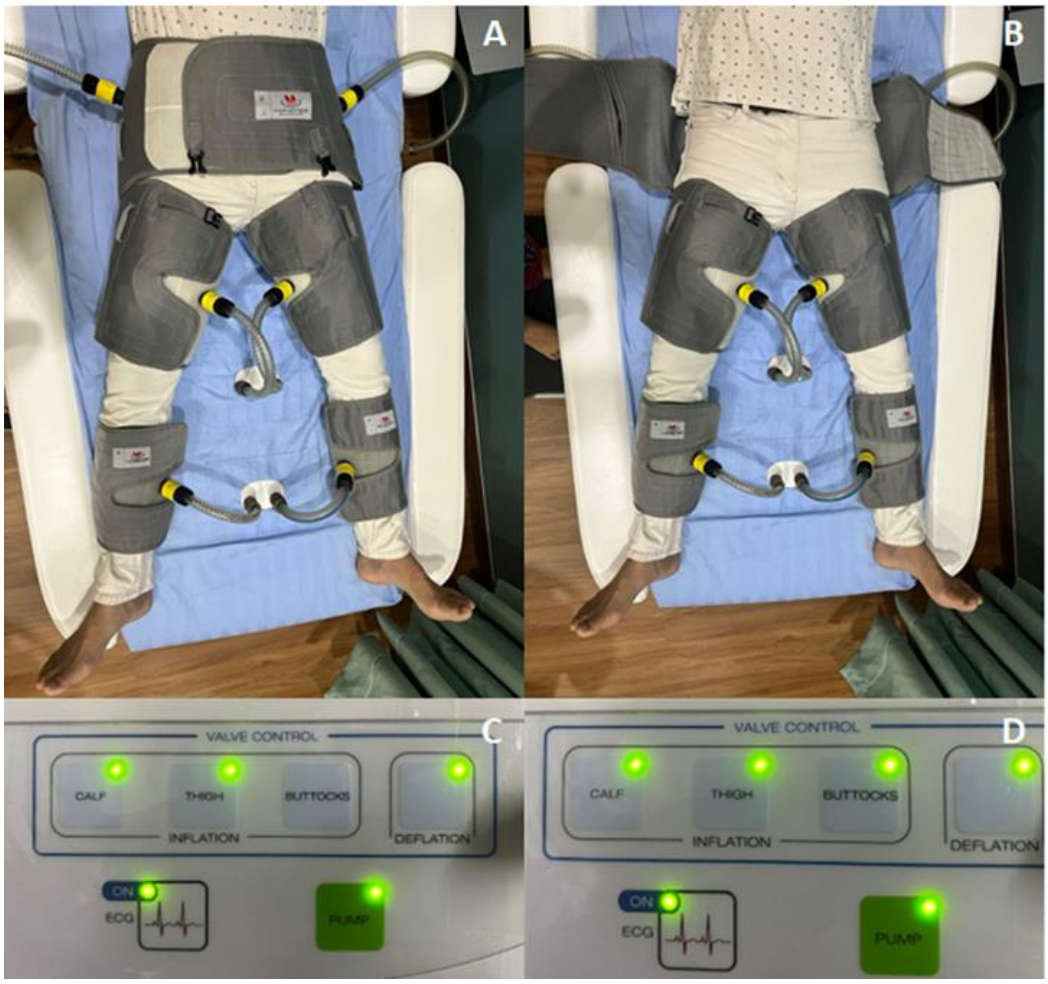

Fig. 3. Three cuff (A) and two cuff (B) ECP protocols. (C) shows the counterpulsation setting on the control panel of a similar device without the buttocks inflation. (D) is three-step counterpulsation setting

xxiv. The straps are applied as tight as possible but should not cause discomfort to the patient.

xxv. Most ECP beds are supine by default and could be reclined accordingly to the comfort of the patient and need of the therapy. Figure 4 shows the front and lateral views of a patient on an ECP device.

Fig. 4. The front and lateral view of a patient on the ECP device

xxvi. The right arm (RA), left arm (LA), and left leg (LL) electrodes should be placed below the right clavicle, below the left clavicle, and closest to the apex, respectively, corresponding to Einthoven's triangle. This is depicted in A) Figure 5.

xxvii. A single-use skin electrode is relatively low in cost for personalised usage on patients.

xxviii. Preferably, the area in which electrodes are to be placed should be cleaned with alcohol or chlorhexidine.

xxix. When needed, the chest may need to be shaven to enhance the ECG signal.

xxx. Jewellery and metal objects along the Einthoven triangle should be removed as they may interfere with the ECG signal.

xxxi. The RA, LA, and LL wires should be attached and applied accordingly to the electrodes.

xxxii. From our clinical experience, the best ECG signals are produced when the electrodes are placed on patients without their tops. This minimises clothing contact with the electrode wires. When this is not possible, a button up shirt is preferred to a T-shirt.

xxxiii. The belt may be loosened or removed as friction may be encountered upon movement of the lower back due to counterpulsation.

xxxiv. The finger probe of the PPG should be applied to the finger that is nearest to the device as depicted in B) of Figure 5.

xxxv. Preferably, the nail bed should be polish-free, or the probe may be applied to either of the ear lobes [52].

xxxvi. Both the PPG and ECG signals are examined and adjusted until they are neither too high nor too low, which may cause clipping or signal loss respectively. The placement of the electrodes can be adjusted accordingly to obtain the best signal possible.

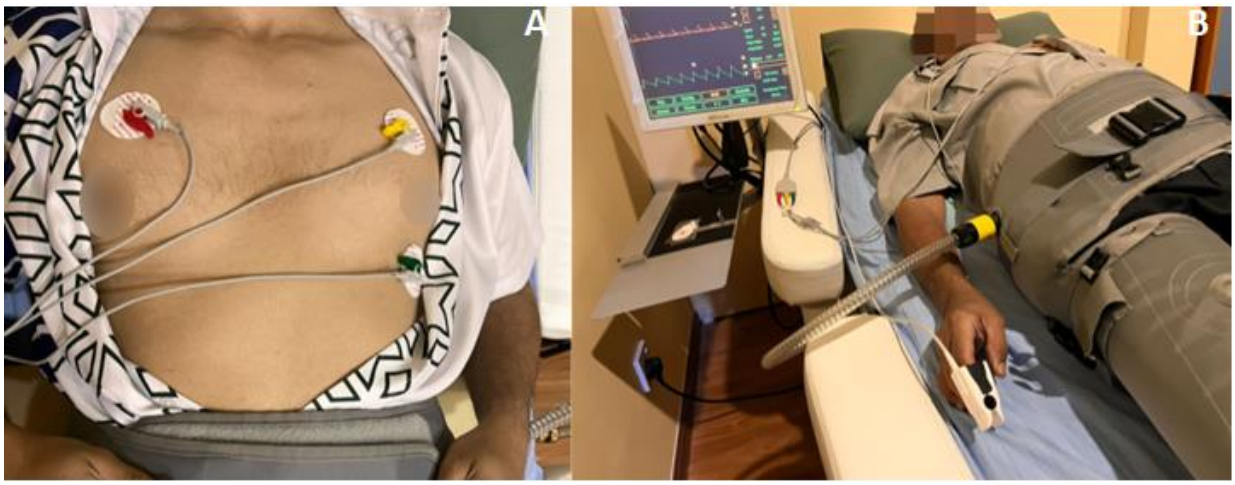

Fig. 5. A) The ECG electrodes placement on the anterior chest wall and B) PPG probe placement on the finger

xxxvii. The data of the patient such as name or ID, number of ECP session, and other relevant data should be stored in the ECP device when feasible. This should be carried out while protecting the privacy of the health data [53]. This should also comply with the local medical data regulation.

2.2.2 During the procedure

i. Treatment time may vary from five minutes to three hours, but most cases are subjected to one hour treatment.
ii. Initially, a single counterpulsation for each two consecutive R waves is advised (1:2).
iii. The cuff pressure is set at 0.017MPa (1 MPa = 7600mmHg) and gradually increased at every two minutes to the point that it is tolerable to the patient.
iv. An example of an ECP operating system is depicted in Figure 6 and Figure 7.

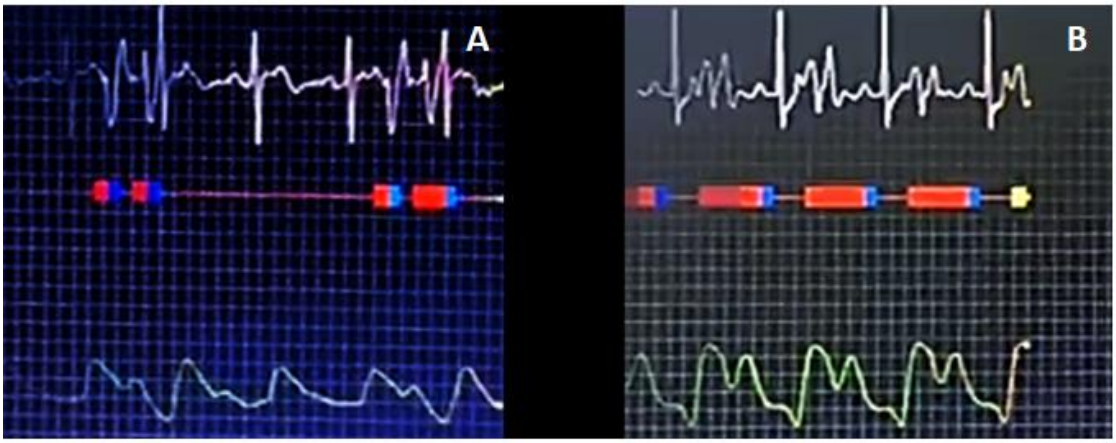

Fig. 6. The ECG (top white waveform), inflation (red square) and deflation (blue square) signals and PPG signal (bottom green signals). A) shows trigger ratio of 3:1 while B) shows 1:1 counterpulsation

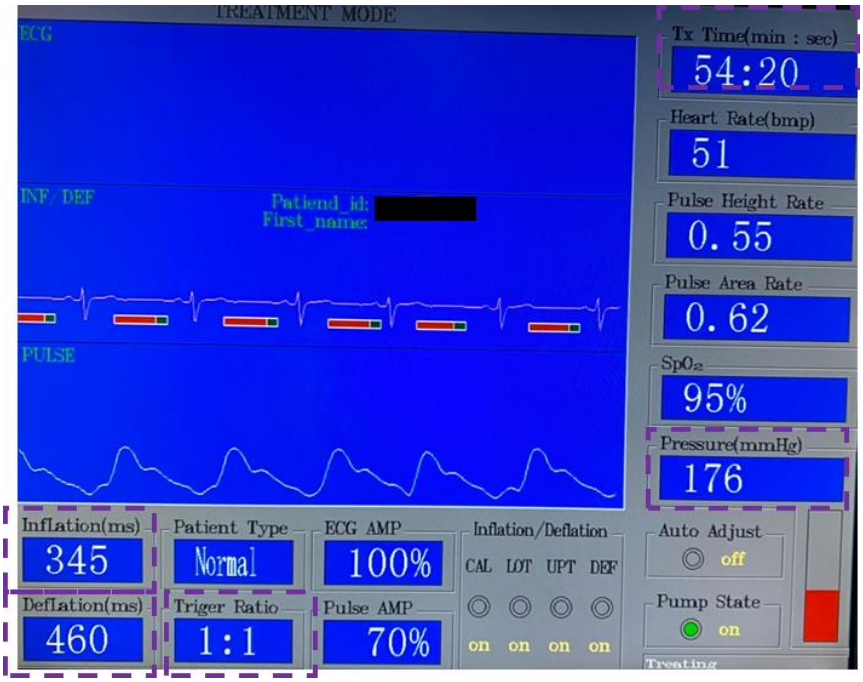

Fig. 7. Example of an ECP system display. The purple dash boxes are parameters that may be adjusted during the ECP treatment

v. The cuff pressure may be gradually increased during each session or at a different session and should not cause pain or additional stress to the patient.
vi. The PPG signal is monitored and optimised to, preferably, an 'M shape', better known as the saddleback pulse waveform.
vii. A good inflation rate should mimic a checkmark (√) sign [36,38].
viii. All the optimal and suboptimal waves and timing errors during inflation and deflation are depicted in Figure 8. These were modified from Ramasamy 2020 [36] and Web *et al.,* [54] respectively.

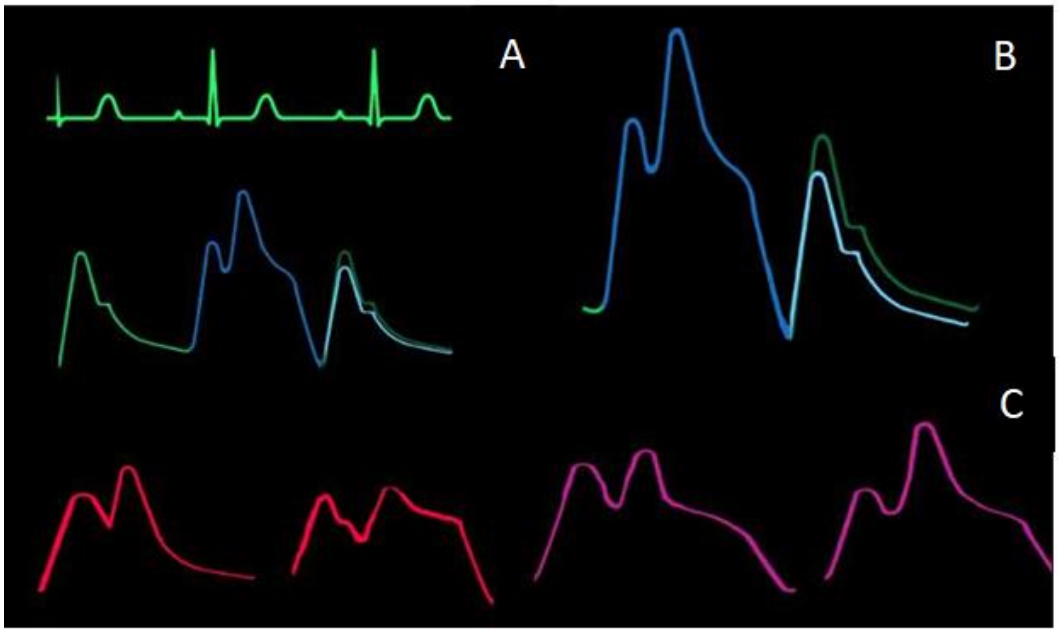

Fig. 8. The optimal and suboptimal waveform(s) of the PPG during counterpulsation. A) PPG during counterpulsation in relation to the ECG. B) Optimal counter pulsation with assisted systolic reduction in the consequent waveform depicted in cyan. C) suboptimal couterpulsation; in red: early inflation, late inflation, in purple: early deflation and late deflation (from left to right)

ix. The cuff pressure and timing of the counterpulsation are targeted so that the diastolic to systolic (D:S) ratio of > 1.2 is achieved at most of the counterpulsation time.

x. Ideally, a pressure of > 0.035 MPa is avoided to reduce discomfort and plausible injury to the skin and muscles. Based on our clinical experiences, the ideal D:S ratio is achieved with < 0.035 MPa. There is also a role for personalised pressure augmentation that has been discussed elsewhere and is beyond the scope of this manuscript [55–57].

xi. In HF cases, higher pressure is recommended. This has been discussed thoroughly elsewhere [24,36,58,59].

xii. After the first 15 or 30 minutes, the trigger ratio may be increased to 1:1, in which the counterpulsation occurs at each pulse beat. It is also vital to note that the trigger ratio may be reduced to 1:2 or lower ratios according to clinical indications such as tachycardia, and patient discomfort.

xiii. The patient should be restricted from touching the ECG electrodes and minimise movement of the hand with the PPG probe.

xiv. Some devices would need manual sampling of the D:S ratio for the final display. This could be achieved by saving the data and conducting post processing of the waves. Ample sampling of these data would be beneficial for documentation, optimisation, troubleshooting, and data analysis purposes.

xv. Adverse events during the ECP should be documented, if any. These include bruises at places where the cuffs were placed.

2.2.3 Post procedure

i. At the end of the session, cuffs are removed, and electrodes are discarded.
ii. The PPG probe and ECG lead are returned to their original placements.
iii. The areas in which the cuffs were placed are examined for any bruises.
iv. Other plausible side effects of ECP include leg or waist pain, ecchymoses, paraesthesia, and worsening of HF in patients with severe arrhythmias [27]. Hence, a thorough assessment is needed even after the ECP session has ended.
v. The post-procedure BP of the patient is recorded, and the lung auscultation is done.
vi. The patient is allowed to go back home if no obvious issues were encountered during the procedure.
vii. The clinician may opt to conduct bio-sampling of weight, body fat, and blood workups right after certain sessions.
viii. The ECP could be repeated as an hour of therapy for 10 sessions or 35 sessions, depending on the indication and clinician's prescription.
ix. The overall workflow during and after the ECP is depicted in Figure 9.

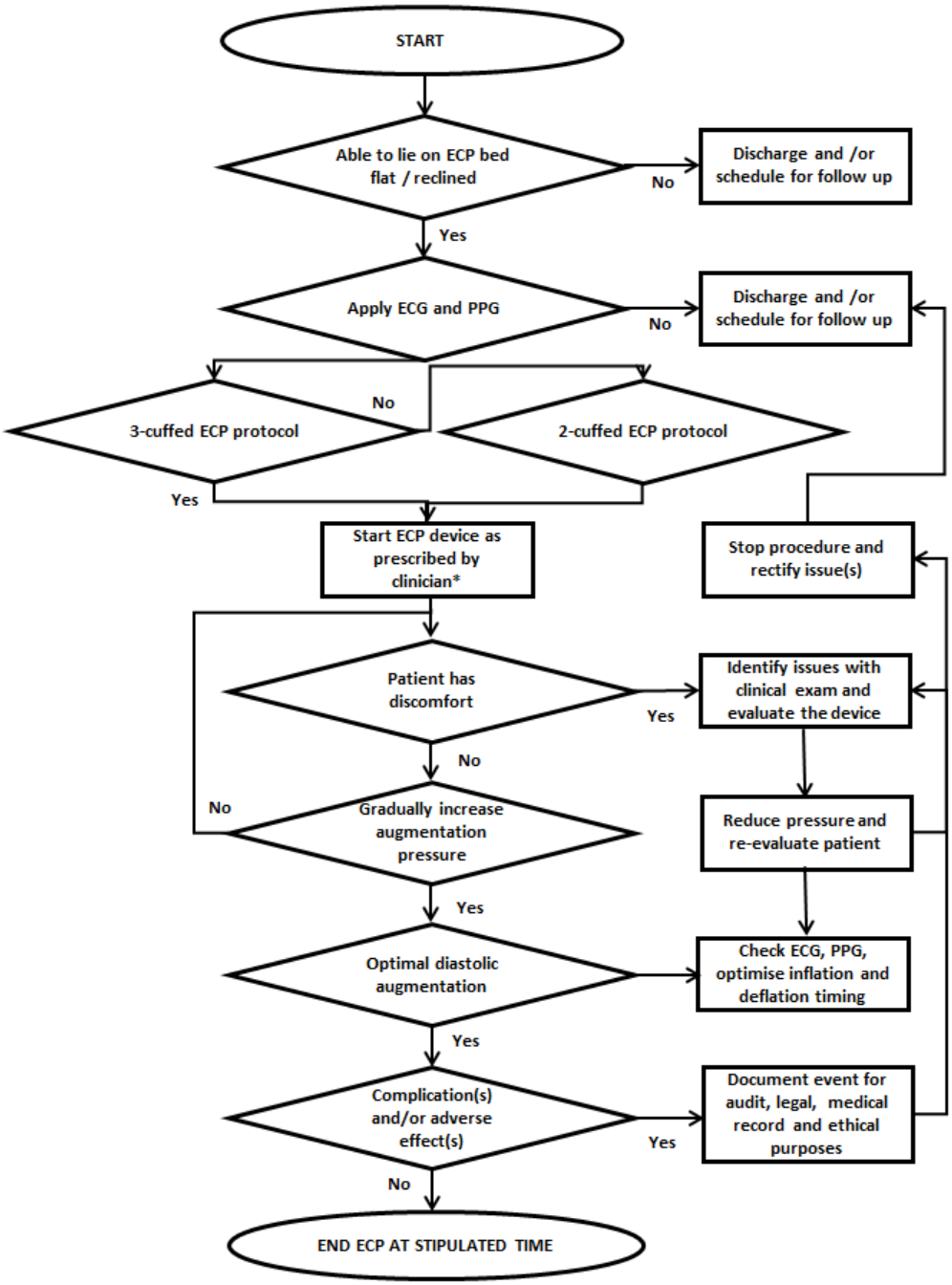

Fig. 9. The proposed workflow during the ECP session. * Indicates that the clinician would determine the number of cuffs to be used, the trigger ratio and cuff pressures for the session

3. Discussion

Expert consensus has recommended that the ECP be conducted 10 or 35 times for maximal benefit [39,60]. This may vary on a case-by-case basis, depending on the different medical conditions and indications. However, it is also common to conduct single or sporadic ECP for post-exercise recovery, peri-cardiac operation optimisation, or other indications [61–65]. Although these studies have studied various durations of ECP ranging between 20 minutes and one hour, a recent article concluded that the benefits for CAD patients are only exerted upon at least 45 minutes of

counterpulsation [66]. As the after-effects of ECP could be assessed at any point of intervention duration, the benefits have been recorded up to three to five years post-ECP [40,67].

The ECP has unique and intriguing supraphysiologic effects on both healthy and diseased subjects [36,38]. This is because the counterpulsation's peripheral effects and properties differ in different arteries, such as the brachial, when compared to the carotids[68] . In addition, a three-cuff versus two- or one-cuff ECP affects the peripheral blood flow and pressure to the lower extremities differently. This has been discussed thoroughly elsewhere [68]. All these knowledge could be put to good use to modulate future ECP-based therapies for other conditions. Advances in a more personalised and precise ECP protocol led to the discovery of individualised shear rate therapy (ISRT). The ISRT is a modified version of ECP that has been successfully used in peripheral artery disease, which were previously contraindicated in ECP [55,56].

ECP improves endothelial function and haemodynamics, improves cardiac function, increases exercise capacity, improves symptoms of angina pectoris, reduces major adverse cardiovascular events and enhances sleep, relieving anxiety and depression [69]. These has been discussed thoroughly elsewhere and is beyond the scope of this protocol paper [69] .

In HF cases, a recent systematic review has shown that the ECP is efficient in reducing hospitalisation rates, improving performance and heart function [70]. The mechanism behind these is contributed by reducing both cardiac load and myocardium loss and enhancing contractility [70]. As the treatment options are limited in ejection fraction preserved heart failure (HFpEF), we postulate that the ECP may be beneficial [71–73]. To back our claims, it is proven that strategies that reduces insulin resistance, improves HbA1C, and sensitises glucagon, could all ameliorate endothelial cell dysfunction [43,74–78]. One of the contributors and consequences of HFpEF is endothelial dysfunction, and therapies targeting this could be game-changing [71–73].

Otherwise, the beneficial effects of ECP are also affected by non-adherence to ECP. A study in China has shown that less than 25% of HF patients adhered to ECP treatment. The same study revealed that those with a higher household income were more likely to adhere to the treatment [79]. One of the contributing factors for the non-adherence also happens to be the distance of the patient's home to the ECP centre. However, we believe that over time, non-adherence may decrease as ECP facilities expand and treatment costs decline.

Most of the adverse effects reported in journals and case reports are equipment related. These are namely leg and back pain, skin abrasion, bruising, blistering, oedema, and paraesthesia. To our best knowledge, there are no reported mortality nor morbidity reported from the usage of ECP in the literature.

It is imperative to pay close attention to how ECP devices are regulated. The legislation pertaining to medical devices should involve local, regional, or international medical device authority [80,81]. The laws, rules, and guidelines regulating the creation, preclinical and clinical testing, and production of the ECP device must be followed by manufacturers. To maintain optimal, if not high levels of care, this should also be carried out during the device's advertising, distribution, and follow-up care. It is noteworthy that the use of electricity and mechanical pumps in the ECP device may pose a risk of fatal injury to the patient. In most countries, the ECP is considered a class I or II device [82]. Furthermore, inaccuracies and timing errors of counterpulsation when done at high pressures no longer exert therapeutic benefits and may in fact be detrimental. To guarantee patient safety and high-quality care, we implore readers of this protocol to utilise approved and regulated ECP devices.

Few of the many limitations to the current ECP devices include it being bulky, not portable and noisy. In addition, there are no clinical methods to measure successful diastolic augmentation nor coronary artery perfusion. ECP devices lack quantitative information on diastolic augmentation as the PPG signals are displayed qualitatively (inflection during diastolic augmentation). Future PPG

devices may address these gaps by quantitatively displaying the normal systolic pressure, assisted systolic pressure reduction, preload pressure, normal diastolic pressure, assisted diastolic augmentation pressure and mean arterial pressure. All the aforementioned could be derived mathematically from the PPG signal. In fact, the systolic pressure time index (SPTI), diastolic pressure time index (DPTI), tension time index (TTI) and subendocardial viability ratio (SEVR) could all be derived from the PPG [36,83,84]. From a clinical perspective, successful diastolic augmentation and increased myocardial perfusion could only be measured via PET-Scan and myocardial contrast echocardiogram (MCE) [85]. These services are not readily available in non-tertiary centres and require special expertise.

As discussed extensively in this manuscript, the ECP has an abundance of benefits and needs a strict protocol. On top of that, this device should be regulated by the medical device authorities of the respected countries and regions to ensure quality control and patient safety. In addition, only trained personnel should handle the device, as the basic knowledge in medical physiology, emergency medicine, internal medicine, cardiology, medical physics, biomedical engineering, and regenerative medicine are required to cater to a wide range of possible issues. These issues include ECP device-related troubleshooting, patient optimisation, and even resuscitation. Furthermore, the health ministry has a role in the legislation of the clinician(s) offering ECP therapy. A trained and certified professional should be the legal and exclusive personnel offering the ECP therapy. Lastly, it is hoped that this manuscript will serve as the blueprint for designing disease- and condition-specific future ECP protocols.

4. Conclusions

In view of the simplicity and availability of ECP worldwide, the authors would like to recommend this protocol for both clinical practice and research purposes. We believe that this protocol will further enhance the capacity and efficacy of the ECP as a regenerative cardiology tool while minimising complications and operator-dependent adverse effects.

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Conflict of Interest
RBM, SRBK are ECP practitioners and owners of ECP centres in Malaysia. AKBM and BV are ECP Practitioners but have no financial interest with any ECP centres in Malaysia. FMM, MJP, VK and BV are ECP and counterpulsation physiology researchers. None of the ECP centre(s), Hospital Sultanah Aminah, Ministry of Health, nor Newcastle University Medicine Malysia (NUMed) were involved in the shaping of this manuscript.

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