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EDITORIAL COMMENT

The AMULET ménage à trois: nurse, telemedicine support, and remote cardiologist

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This article refers to 'Effects of an outpatient intervention comprising nurse-led non-invasive assessments, telemedicine support and remote cardiologists' decisions in patients with heart failure (AMULET study): a randomised controlled trial' by P. Krzesiński *et al.*, published in this issue on pages 565–577.

When considering telemedicine in heart failure (HF), we have in mind remote patient monitoring with a daily transfer of vital parameters from patient's home to caregivers. The main purpose of this approach is the prevention of HF hospitalizations due to early detection of a cardiac decompensation and an immediate response. The concept of home telemonitoring was investigated in several randomized controlled trials (RCTs) using different invasive and non-invasive devices. The results of these RCTs are inconsistent (*Table 1*).

AMULET was a multicentre, prospective, randomized, open-label, controlled, parallel group trial investigating the efficacy of a telecare model based on nurse-led outpatient service at so-called 'ambulatory care points' (ACPs).[10] The study was performed in nine sites in Poland between March 2018 and October 2020.

The basic concept of the AMULET telecare model is a nurse-led HF outpatient service combined with telemedical support by a cardiologist. The nurses assessed HF signs and symptoms during seven outpatient visits during 12 months of follow-up at the ACP. During these visits, additional vital parameters – heart rate, blood pressure, thoracic fluid content, body mass and total body water – were measured using body impedance and impedance cardiography techniques. All information obtained was sent to a cardiologist using web modules including recommendation support to allow clinical interpretation of visit-to-visit changes of the body impedance and haemodynamic parameters. Resulting therapeutic decisions made by the cardiologists were sent back to the nurses. The nurses provided this information to the patients and recommended to follow this advice.

The hardest difference regarding the telemedical setting between AMULET and home telemonitoring studies is the lack of devices at patient's home, resulting in a reduced number of transferred vital parameters during the seven visits only.

The patients in the control arm were followed by cardiologists and other physicians in the 'real-life' healthcare system with no fixed protocol regarding follow-up visits except for the baseline visit and the final visit after 12 months.

The study population included 605 patients with a left ventricular ejection fraction (LVEF) <50% and with at least one episode of HF hospitalization within 6 months prior randomization. Nearly 60% of the patients were 65 years or older. All patients were assigned either to the AMULET telecare group (n = 300) or to the control group (n = 305). The rate of premature resignation from the intervention was 3.7% (n = 11), which is within the usual range of other telemedical studies in HF.[1–4]

The primary endpoint of AMULET was a composite of the first unplanned HF hospitalization or cardiovascular death during 12-month follow-up. There were eight secondary endpoints, e.g. cardiovascular death, first unplanned HF hospitalization and total number of HF hospitalizations. Of note, no patient-centric endpoints such a quality of life or self-care behaviour were investigated. There were seven pre-specified subgroups, e.g. the comparison between high-reference centres/university clinics and district hospitals/outpatient specialist clinics. The nine sites included four university clinics, which enrolled 410 patients (68%) whereas the two district hospitals and three outpatient specialist clinics enrolled 195 patients (32%).

The study met its primary endpoint, which was driven by a significant lower incidence of HF hospitalizations. There were no differences in cardiovascular or all-cause mortality. The highest efficacy regarding the primary endpoint was shown in ACPs, which were connected to cardiologists located in district hospitals or in outpatient specialist clinics.

The stable study population represents an important aspect when interpreting the trial results. Although at least one event

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Table 1 Contemporary randomized controlled trials investigating remote patient monitoring

Study acronym	No. of patients	Country/area	Primary endpoint
RPM with non-invasive telemonitoring			
TIM-HF[1]	710	Germany	Neutral
BEAT-HF[2]	1437	USA	Neutral
TIM-HF2[3]	1538	Germany	Positive
OSICAT[4]	937	France	Neutral
RPM with invasive telemonitoring			
CHAMPION[5]	550	USA	Positive
IN-TIME[6]	716	Europe, Israel, Australia	Positive
OptiLink-HF[7]	1002	Germany	Neutral
REM-HF[8]	1650	UK	Neutral
GUIDE-HF[9]	1006	USA, Canada	Neutral

RPM, remote patient monitoring.

of HF decompensation within 6 months prior to randomization was a key inclusion criterion, defining a higher risk for the primary endpoint, 76% of patients were in New York Heart Association functional class I and II at baseline, resulting in a low risk for rehospitalization and premature death. Therefore, the total number of alerts was low with only 77 'red flag' alerts requiring an in-person contact with a physician within 2 h according to the study protocol. This is a very low event rate of 0.25 emergencies/patient-year. In both TIM-HF and TIM-HF2, the event rate was 0.56 emergencies/patient-year.[11]

Nevertheless, AMULET is one of the first positive trials addressing the increasing problem of providing guideline-based HF care, in particular to patients living in rural areas with limited access to high-volume HF centres. This model investigated the delegation of HF care to a trained nurse supported by a bi-directional telemedical support. The nurse-led HF care model investigated in the AMULET study is new, not only for the Polish healthcare system, and significant effects in reducing HF hospitalizations could be shown.

Another promising approach is a pharmacist-led interdisciplinary intervention for HF outpatients.[12] The PHARM-CHF RCT showed that pharmacy care safely improved adherence to HF medications and quality of life as well as drug therapy but was underpowered to detect an intervention effect on morbidity/mortality.[13,14]

Due to the novelty of the AMULET concept, some relevant questions have to be answered before implementation in a real-world setting:

- Has a tele-cardiologist to work as an onsite physician who knows the patients from previous face-to-face appointments or can the tele-cardiologist work in another HF centre without prior direct patient contact?
- If the latter, does this cardiologist must have real-time access to the entire patient medical history and files?
- What should be the optimal/realistic response time between sending data to the tele-cardiologist and receiving feedback?
- What can trained nurses do themselves without tele-consultation of the cardiologist?
- What is the role of the primary care/family physician and who is prescribing the drugs recommended by the tele-cardiologist?

Another important aspect not specifically addressed by AMULET is the need for a better patient profiling for any telecare model in HF. It seems that not every patient recently hospitalized due to HF needs home telemonitoring with a daily review of vital parameters. Differences in patient profiling can be considered as one important reason for the inconsistent results between previous home telemonitoring studies (*Table 1*). Positive telemedical RCTs in HF required inclusion of a high-risk group of HF – that is, patients recently hospitalized for decompensated HF. So, it is not surprising that the AMULET authors discuss the option of combining their telecare model with home telemonitoring for specific patients.

Since the beginning of 2022, home telemonitoring is reimbursed for functional class II and III patients with a history of HF hospitalization and a LVEF <40% in Germany, opening the access for digital support in HF care for approximately 150 000 eligible patients.[15]

The evidence of the AMULET study supported by the upcoming real-world data following wide-scale implementation suggests that any upcoming care model in HF will include a digital component.

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