

The Gap In Meeting The Educational And Support Needs Of Women With Takotsubo Syndrome Compared To Women With An Acute Coronary Syndrome

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ABSTRACT

Background: Takotsubo Syndrome is a condition that causes impairment in cardiac function in the absence of significant causative coronary artery disease. Takotsubo Syndrome is most commonly reported in older women, has identical presenting symptoms to acute coronary syndrome (ACS), but differs in cause, management and outcomes. Ongoing symptoms and recurrence of Takotsubo Syndrome are not uncommon but little support is available for these women.

Aims: This study compares (1) educational support and (2) participation rates in outpatient cardiac rehabilitation for women with Takotsubo Syndrome or acute coronary syndrome, and (3) ascertains whether or not they perceived similar benefits from these strategies.

Methods: 23 women with Takotsubo Syndrome and 23 age-matched women with acute coronary syndrome were mailed a structured questionnaire based on cardiac rehabilitation (CR) components.

Findings: The questionnaire response rate was 48% (n=11) for the Takotsubo Syndrome group and 30% (n=7) for the acute coronary syndrome group. 18% (n=2) of the women with Takotsubo Syndrome and 71% (n=5) of the women with acute coronary syndrome attended cardiac rehabilitation, with all attendees perceiving that it was beneficial in aiding their recovery. Of the nine women with Takotsubo Syndrome that did not attend cardiac rehabilitation, 67% (n=6) perceived that it would have been helpful in aiding their recovery. Women with Takotsubo Syndrome were less likely to receive educational support about their condition, particularly stress management and participate in CR compared with women with ACS, despite perceiving that elements of CR would have been helpful in aiding their recovery.

Conclusions: Women with ACS had higher CR participation rates than those with Takotsubo Syndrome, and were more likely to receive educational support, particularly following hospital discharge. The majority of women with Takotsubo Syndrome were not exposed to educational support in their recovery, suggesting a role for CR tailored to the needs of these women. Nurses can take practical steps to address these gaps by providing emotional support and education for women with Takotsubo Syndrome in stress management to enhance their quality of life and reduce potential recurrence.

Keywords: Takotsubo; Stress; Anxiety; Cardiac Rehabilitation; Patient Education

INTRODUCTION

Takotsubo Syndrome (TS) is a condition that causes impairment in cardiac function in the absence of significant causative coronary artery disease (Yoshikawa, 2015). Onset of TS is in most cases associated with an acute physical or emotional triggering event, and 85-90% cases reported to date are in postmenopausal women (Sharkey & Maron, 2014). The initial clinical presentation for TS is indistinguishable from that of acute coronary syndrome (ACS), and includes symptoms of chest pain, dyspnea and occasionally cardiac arrest. The troponin is elevated and an electrocardiogram (ECG) may show ST-segment elevation, T-wave inversion, or no apparent abnormalities. It is estimated that 10% of women presenting to hospital with suspected ACS ultimately receive a diagnosis of TS (Lyon et al. 2016; Deshmukh, Kumar, Pant, Rihal, Murugiah & Mehta, 2012). Although TS mimics ACS at initial presentation, the pathophysiological mechanisms for the two conditions are different (Akashi, Nef, & Lyon 2015). It is generally accepted that catecholamines have a role in the development of TS, but the pathophysiological mechanism is poorly understood (Lyon et al. 2016).

Whilst there are well-defined evidence-based strategies for managing ACS (Amsterdam et al. 2014; Roffi et al. 2015), this is not the case for TS (Omerovic, 2016). Patients presenting to a hospital emergency service with TS generally receive 'default' ACS management (Lyon et al. 2016) followed by symptom-guided care in hospital once TS has been diagnosed (Jayasinghe & Khan, 2015). Support and information about TS during hospitalization and following hospital discharge is scant for women with TS. The diagnosis of TS is not only unfamiliar to them, but also to most of the healthcare professionals that they encounter in the hospital and the community (Dahlviken, Fridlund & Mathison, 2015). They are often erroneously told that TS is a self-limiting, benign condition from which they will recover quickly and completely, and have no options for obtaining reliable advice and information about the condition. Very few community health practitioners have experience in managing patients with TS, and if they do know what TS is, they are generally unaware that TS can recur or be associated with ongoing symptoms. Thus, symptoms are dismissed by health professionals as stress and anxiety. Thus, it is not surprising that anxiety states are common in women with TS (Lyon et al. 2016). In contrast, ACS has well-established guidelines for management and secondary prevention following hospital discharge. Cardiac rehabilitation (CR) begins in hospital with education, followed by exercise-based outpatient CR and secondary prevention that focuses on cardiac risk factor reduction for patients with ACS. CR has been shown to significantly reduce cardiovascular mortality and hospital admissions and is associated with improved QoL (Anderson et al. 2016). Recent evidence suggests that women with TS do have a need for support and education similar to that offered in CR programs, but it appears that this is not routinely available to them (Dahlviken et al. 2015).

BACKGROUND

In the majority of studies reported to date, a key feature of TS has been the rapid resolution of regional left ventricular (LV) wall motion abnormalities and recovery of LV function, normally within six weeks for the majority of people. This has led to a widespread, but flawed view that TS is a 'relatively benign curiosity with an excellent long-term prognosis' (Neil et al. 2012). It is becoming increasingly evident that this is not the case. As longer-term data accumulates, it is clear that mortality rates in TS are higher than previously thought (Stiermaier et al. 2016). During the acute in-hospital phase for TS, mortality is comparable with that for ST-segment elevation myocardial infarction (STEMI), and following hospital discharge, is higher in TS than in an aged-matched healthy population (Akashi et al. 2015).

Rates of recurrence for TS has been estimated to be as high as 22% (Akashi et al. 2015). Wallström, Ulin and Omerovic (2016) compared self-reported symptoms 8 weeks after hospital discharge for women with TS and ACS, and found that both groups experienced fatigue, sleep disturbance, and exertional dyspnoea to a similar degree, and these symptoms had a negative impact on quality of life (QoL) for both groups. Women, in particular, often have persistent symptoms including fatigue, chest pain, exertional dyspnea, and palpitations 12 months after the initial TS diagnosis (Stiermaier et al. 2016; Wallström, Ulin, Omerovic, & Ekman, 2015, and in some, the symptoms never resolve completely. This may be explained in part by findings of a recent study (Schwarz et al. 2017) that found despite apparent normalisation of global LV function, some patients with the most clinically severe spectrum of TS had persistent LV abnormalities well beyond the acute event due to global microscopic fibrosis that develops as TS-related

intramyocardial edema resolves. The issues of delayed or incomplete recovery of patients with TS and frequent recurrence of TS suggest that there may be a form of ‘chronic’ TS (Madias, 2016).

There are good reasons why women with TS should receive up-to-date and accurate information about their condition. They (as well as their family and support network) need an explanation of what TS is and current information as to why it occurs. They need to know what to expect following hospital discharge: how to safely manage medications; what to do if they experience ongoing symptoms or recurrences of TS; how to minimise their risk of recurrence. Clinicians are uncertain whether CR, or components of CR are likely to have any benefit for women with TS, and so the practice of CR referral for patients with TS is institution-dependent. ACS is associated with a range of recognized risk factors that are modifiable and have therapeutic targets for secondary prevention. With the exception of psychological stress, there is currently no evidence of an association between these traditional risk factors for cardiovascular disease and TS.

METHODS

A survey method was chosen because it was simple to complete, minimized burden to participants, and suited the quantitative and qualitative components of the study. Participation was limited to women with TS or ACS in the preceding 12 months as the reliability of patient recall of events decreases with time, as do questionnaire response rates (Thorn et al. 2013).

Study Aims

The aims of this study were to compare (1) educational support and (2) participation rates in outpatient CR for women with TS or ACS, and (3) ascertain whether they perceived similar benefits from these strategies in aiding recovery. We defined ‘aiding recovery’ as being ‘an action, information or procedure that you feel helped you to recover from your cardiac condition.’

Participant Sample

Purposive sampling was used to identify two groups of participants. The TS Group included all women ≥ 18 and ≤ 85 years of age with a first episode of TS in the preceding 12 months (September 2014 – October 2015) who had previously participated in a study of TS in Australia. The study was conducted at a metropolitan hospital and included women presenting to, or transferred to, the study hospital and two other metropolitan hospitals. The ACS Group consisted of a group of women age-matched to the TS cohort with a first episode of ACS from the study hospital over the same period. Sample size was determined by the number of women with TS eligible for study inclusion. Males were not included in this study as they represented a small portion of this cohort and had TS secondary to a serious physical illness, making them unlikely candidates for CR. Women >85 years of age were not included in the study as they were also less likely to be referred to a CR program.

Ethical Considerations

The investigation conforms to the principles outlined in the Declaration of Helsinki (Rickham, 1964) and was approved by both the University and relevant hospital ethics committees. Questionnaires were accompanied by a letter with information about the study and advising that a completed and returned questionnaire would indicate consent for information provided to be used in the study.

Data Collection

Instrument

Eleven key survey questions were structured around fundamental CR activities including explanations about the condition, psychological support and counseling, education on risk factor reduction and new medications, and exercise (Woodruffe et al. 2015). Participants were asked to indicate whether or not they were exposed to individual CR activities and if so, where this occurred (in hospital, in an outpatient CR program, or elsewhere following hospital

discharge). Participants were then asked to give an indication of how helpful they perceived the exposure to the activity to be in aiding their recovery; or, if they had not been exposed to the activity, how helpful they perceived it would have been in aiding recovery had they been exposed to the activity. They could indicate ‘helpful; ‘not helpful’; or ‘unsure’ in response to each question.

Data Analysis

Proportions, means and standard deviations (SDs) were used to describe TS and ACS samples. Non-paired t-test was used for inter- and intra-comparisons of mean age in TS and ACS groupings. Fisher's exact test of independence was used for nominal variables between groups for questionnaire responses relating to exposure to elements of CR. Proportions were used to describe survey responses of perceived utility of the CR elements.

RESULTS

There were 44 patients diagnosed with TS in the study period. Of these, 40 (91%) were female, consistent with the currently reported gender demographic for TS (Minhas, Hughey, & Koliass, 2015). Eight women (20%) were >85 years and thus did not meet inclusion criteria; a further nine had exclusion criteria. Survey questionnaires were sent to 23 women in the TS Group (mean age 68.4+/-10.0 SD) and 23 age-matched women with ACS (mean age 66.9+/-10.0 SD). Notably, 11 (48%) of the TS Group (mean age 67.4+/-11.7 SD) completed and returned the questionnaire compared to 7 (30%) of the ACS Group (mean age 69.4+/-7.9 SD). There was no significant difference in survey response rate, or in mean age between women to whom questionnaires were sent and women who completed the questionnaire (responders) in intra- and inter-group comparisons.

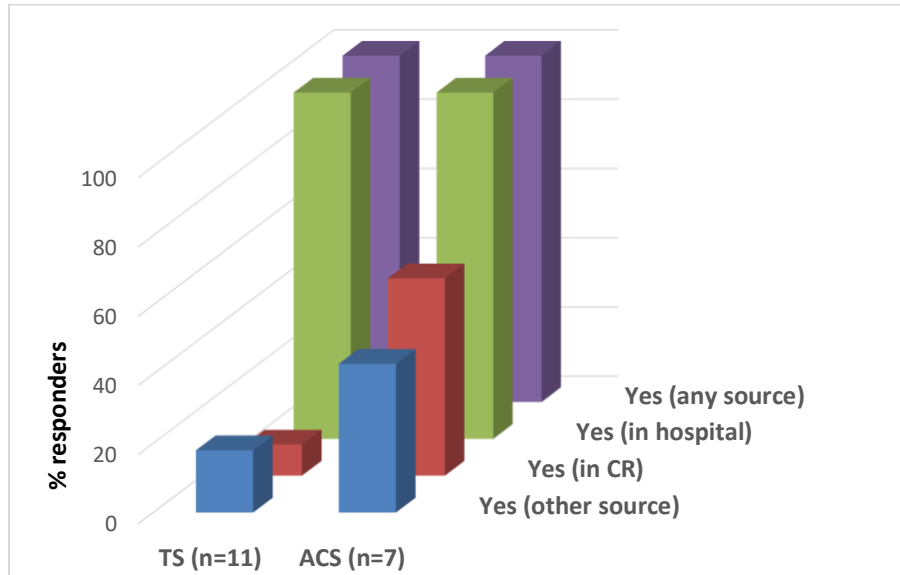
Outpatient CR Program Attendance

ACS responders were more likely to have attended an outpatient CR program compared with TS responders (71% vs. 18% respectively; $p=0.04$). Five (45%) TS responders had not been invited to attend an outpatient CR program and the reason for non-attendance in the remaining four was not recorded by participants. Two ACS responders who did attend CR were invited to do so but had unexpected medical events. All women who attended CR perceived it to be beneficial in aiding recovery. Of the nine TS responders who did not attend CR, six (67%) perceived that it would have been helpful in aiding recovery.

Explanation of the Medical Condition

All responders from both groups received an explanation of their medical condition in hospital (see *Figure 1*), but compared with TS responders, ACS responders were more likely to receive further information about their medical condition after hospital discharge ($p<0.01$). Six (55%) of the TS and six (86%) of the ACS responders perceived that receiving an explanation of their medical condition was helpful in aiding their recovery.

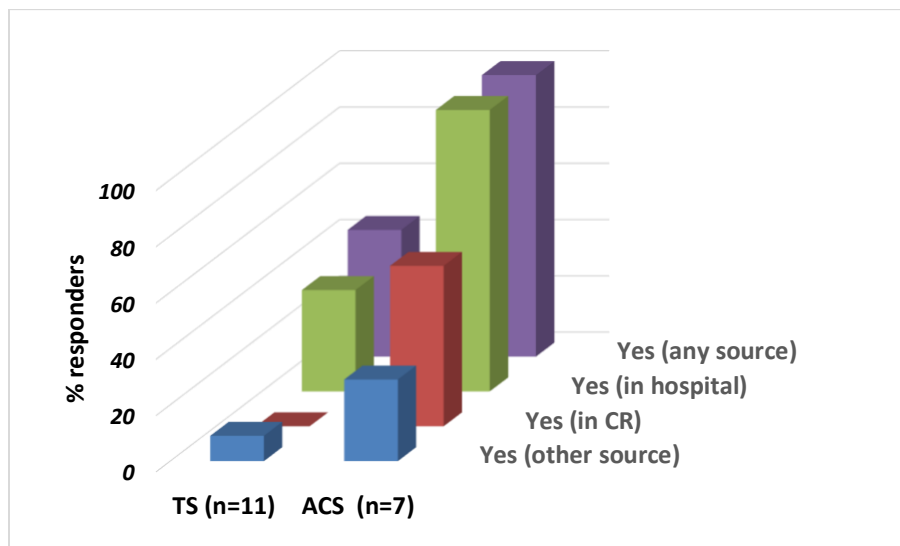
Figure 1. Comparison of TS and ACS responders receiving an explanation of the medical condition and source of information



Information About How the Medical Condition May Affect Normal Life Activities

Figure 2 shows that only five (45%) of the TS responders reported receiving information about how their medical condition may affect their normal life activities compared to 100% (n=7) of ACS responders (p=0.04). Four (36%) of TS responders received this information in hospital and one from a research nurse following discharge. Four (57%) of the ACS responders gained further information in CR and two (29%) from their cardiologist. All (100%) of ACS responders and four of the five (80%) TS responders who received this information perceived it to be helpful in aiding their recovery. Five of six (83%) TS responders that were not given this information perceived that it was likely to have been helpful in aiding recovery.

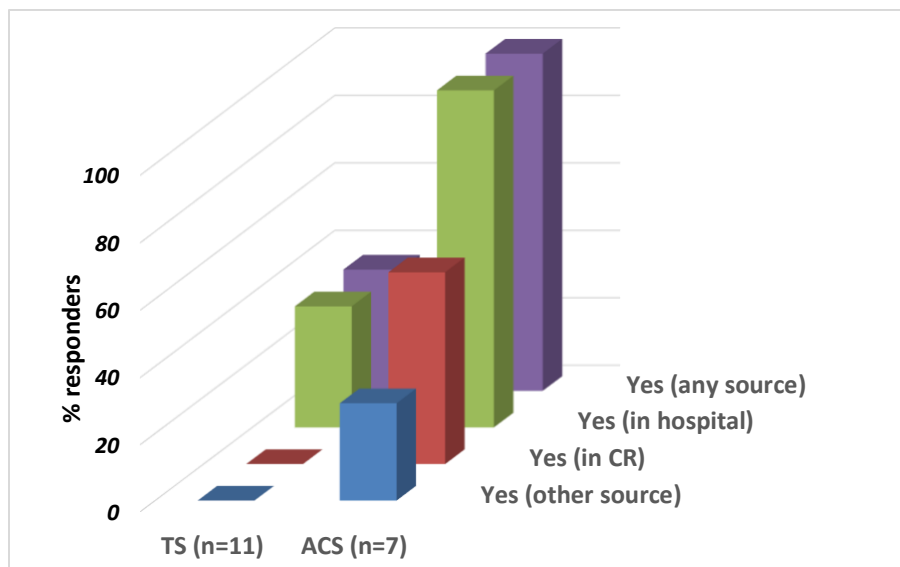
Figure 2. Comparison of TS and ACS responders receiving information of potential effect of TS on normal life activities and source of information



Information on Managing Another Episode of the Medical Condition

Only four (36%) TS responders received information on how to manage another episode of their medical condition, whilst all 7 (100%) ACS responders did so ($p=0.01$) (see *Figure 3*). The primary source of this information for TS responders was in hospital, while four of the ACS responders received further information in a CR program (57%) and two (29%) from their cardiologist. All responders that received information on how to manage another episode of their medical condition perceived this to be helpful in aiding their recovery. Five (71%) TS responders not having received this information said that it was likely to have been helpful in aiding recovery.

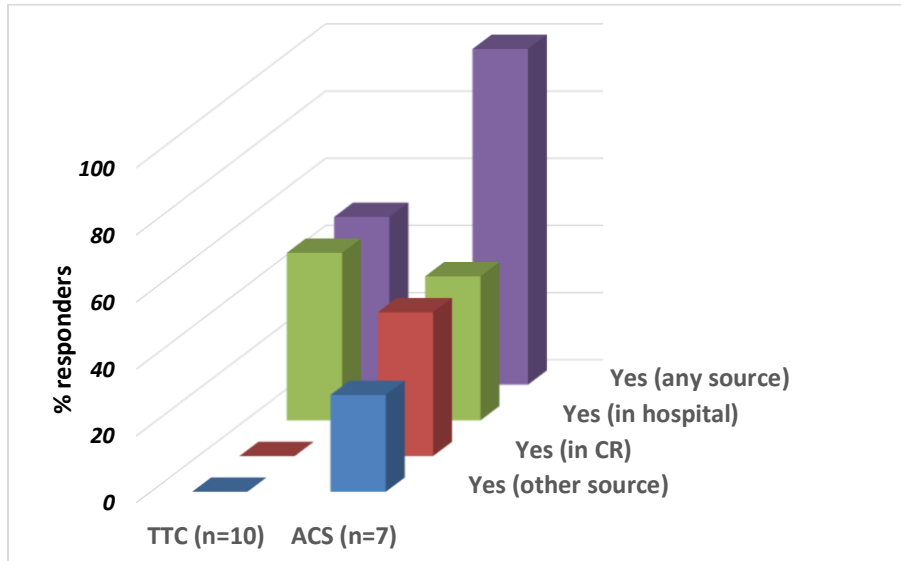
Figure 3. Comparison of TS and ACS responders receiving information on how to manage a recurrent episode and source of information



Medication Advice

One TS responder reported that she had not started any new medication. Five (50%) of the remaining TS responders reported receiving advice/information about new medication compared with 100% of ACS responders ($p=0.005$) (see *Figure 4*). All five TS responders received this information in hospital only. Three (43%) of the ACS responders received this advice in hospital, three (43%) in a CR program and two (29%) from their GP or cardiologist (one patient reported receiving information from more than one source). All (100%) of the ACS responders received this advice and all (100%) perceived this to be helpful in aiding recovery. 80% of the TS responders that received medication information perceived this to be helpful in aiding their recovery and 60% of those not having received this information perceived that it would have been helpful in aiding recovery.

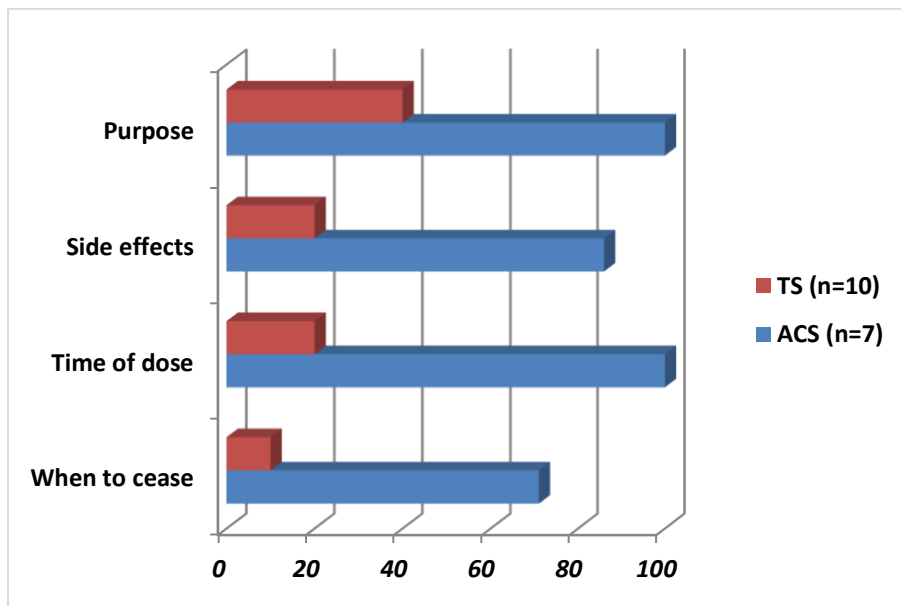
Figure 4. Comparison of TS and ACS responders receiving medication advice and source of information



*One responder reported gaining information from two sources.

The purpose of the new medication was explained to only 40% (n=4) of the TS Group responders and 100% (n=7) of the ACS Group responders (p=0.03). Side effects, actual or potential, were explained to 20% (n=2) of the TS Group responders and 86% (n=6) of the ACS Group responders (p=0.01). When to take a dose of the medication(s) was specified to 20% (n=2) of the TS Group and 100% (n=7) of the ACS Group (p=0.002). Finally, when to cease taking the medication was explained to 10% (n=1) of the TS Group and 71% (n=5) of the ACS Group (p=0.03) (see Figure 5).

Figure 5. Comparison of TS and ACS responders receiving specific medication advice/information



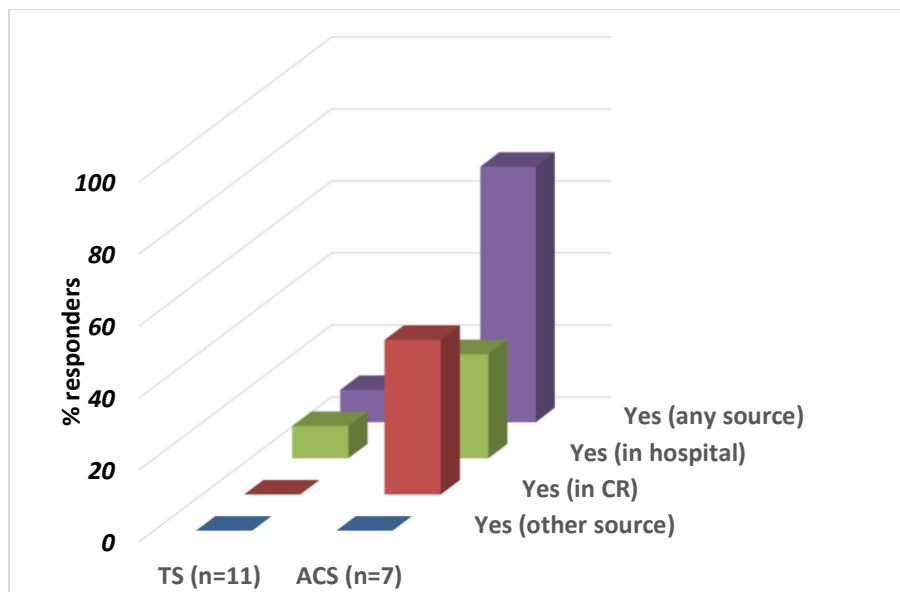
Counselling on Risk Factors for Heart Disease and Lifestyle Advice

100% of ACS responders received counselling about risk factors for heart disease and lifestyle advice compared to five (45%) TS responders ($p=0.04$). Although we collected data on all risk factor information proffered, the risk factors that are likely to have the most impact on women with TS are stress, anxiety and depression, and we present data relating to these here.

Managing Stress, Anxiety and the Feelings of Depression

Figure 6 shows that only one of the TS responders was counseled on managing feelings of stress, anxiety and depression compared to five (71%) of the ACS responders ($p=0.01$). The source of this counselling was only given whilst in hospital for the patient with TS. The ACS responders obtained this information during their hospital stay (43%) or in a CR program (29%). All responders that received counseling on managing stress, anxiety and depression believed it was helpful in aiding their recovery. For the TS responders that did not receive counseling, 80% perceived that it would have been helpful in aiding their recovery.

Figure 6. Comparison of TS and ACS responders receiving counselling on managing stress, anxiety and depression



DISCUSSION

Little is known about information and support offered to women following an episode of TS, but it appears that there is very little is available (Dahlviken et al. 2015). There is good evidence that CR and secondary prevention strategies following a cardiac event decreases morbidity and mortality, and improves QoL for patients with CVD (Dalal, Doherty & Taylor, 2015). In addition to addressing secondary prevention through modification of biomedical risk factors, the impact of stress, anxiety and depression on the development of CVD, as well as poor outcomes following a cardiac event (Steptoe & Kivimäki, 2012; Cohen, Edmondson & Kronish, 2015) has gained increasing interest and acknowledgement. Stress reduction and the management of stress-related conditions aid recovery from an acute cardiac event (Yohannes, Doherty, Bundy & Yalfani, 2010), thus, stress reduction is a major component of CR programs. Other aspects of CR may incrementally contribute to psychological wellbeing. A study by Blumenthal et al. (2012) showed that exercise was equal to pharmacological management with sertraline in reducing depressive symptoms compared to placebo in patients with CHD. CR also discourages maladaptive stress-coping strategies, such as tobacco and alcohol use, sedentary activities, and unhealthy eating behaviours which may contribute to overall ill health and promotion of chronic disease that has potential to cause further stress.

Medication advice is also an important component of CR. To date there is no validated evidence for standardized pharmacological management of patients with TS following hospital discharge, but it is common practice for antithrombotic and heart failure therapy to be prescribed for at least the first two months (Abanador-Kamper et al. 2017). The majority of patients with TS will be discharged from hospital with a new medication regimen. Beta blockers and angiotensin converting enzyme-inhibitors or angiotensin receptor blockers will be prescribed for the majority of patients; additionally, mono or dual antiplatelet therapy, mineralocorticoid receptor antagonists and statins may be prescribed for some. As there is no convincing evidence that these drugs promote recovery or prevent recurrence of TS (Abanador-Kamper et al. 2017; Lyon et al. 2016), it may be difficult to explain the purpose of the taking the medication and risks of taking/not taking the medication to patients, but at the very least, they need to be informed about when and how to take the medications; interactions associated with the medications; recognizing side effects and taking appropriate action should they occur; and storing the medication.

Exercise-based CR has been shown to provide important health benefits including reductions in cardiovascular mortality, hospitalization and associated health care costs, and improvements in health-related quality of life (Anderson et al. 2016). A recent study suggested that women with heart disease derived a greater mortality benefit from attending CR compared to men, though women were less likely to be referred and less likely to attend CR programs (Colbert et al. 2015).

Women with TS are not routinely offered CR, and this may be at least in part due to current gender biases in referral patterns and attendance at CR for women overall. Women with TS in this study were less likely than those with ACS to be referred to CR, and less likely to attend an outpatient CR program. The question of whether CR may be useful in decreasing the rates of recurrence, morbidity or mortality in TS has not yet been examined. In a climate of stretched resources, where many CR services report that there is insufficient capacity to include all currently referred patients, CR clinicians may feel that efforts should be concentrated where there is strong evidence of benefit, and this is predominantly in patients with CVD.

Emerging evidence indicates that Takotsubo is a syndrome with a significant risk of recurrence (Kato, Kitahara & Kobayashi, 2016; Singh et al. 2014) and lingering symptoms that can severely impair QoL. As observed by Dahlviken et al. (2015), women with TS require education and counselling from healthcare professionals to help them to comprehend and manage having a TS diagnosis. Stress management and counseling may have a role in reducing recurrence triggered by emotional stressors, especially in women with confirmed anxiety disorder (Lyon et al. 2016) that appears to be prevalent in women with TS (Goh, Wong, Zaroff, Shafae & Lundstrom, 2016; Wallström, Ulin, Määttä, Omerovic & Ekman, 2016). Participation in CR has been shown to reduce anxiety, depression, lack of self-confidence, emotional stress, and social isolation, whilst improving psychological functioning and QoL (Woodruffe et al. 2015). CR is now indicated for patients with a range of cardiac disorders, leading to a diverse array of CR services tailored to an individual's needs and capabilities (Woodruffe et al. 2015). Healthcare professionals can provide education and counselling for people with TS and foster self-care habits to mitigate stress and potential recurrence.

In the past decade, researchers have made a great deal of progress in recognising the population demographic most prone to developing TS, new variants of TS, various triggers for TS, and useful diagnostic tests to identify TS. The cause and pathophysiology of TS is still incompletely understood, but recognition of an element of chronicity in this condition has led to a gradual change in nomenclature from 'Takotsubo cardiomyopathy' to 'Takotsubo syndrome' and has important implications for current perceptions of morbidity and mortality and the need for ongoing support for those with the condition.

LIMITATIONS OF THE STUDY

There were a few limitations in this study. Survey response rates were 48% and 30% for the TS and ACS groups respectively. Whilst it would have been desirable to have higher response rates, there were significant differences in the question responses between the groups. Eight women (20% of the original sample of 44 patients with TS in the preceding 12 months) were over 85 years and were excluded based upon the difficulty of matching them to ACS patients attending an exercise-based CR program. Thus, further research studies are required to ascertain the rehabilitation needs of older women with TS, as well as males who were also excluded from this study. Finally, the

ACS Group were purposefully sampled for having agreed to attend an outpatient CR program, and this may represent a group of patients that have a more positive attitude to CR compared to those ACS patients who choose not to attend, potentially resulting in bias regarding perceived benefit of CR.

IMPLICATIONS FOR CLINICAL PRACTICE AND RESEARCH

- Compared with women with ACS, women with TS receive significantly less support and education about their condition. Women with TS are less likely to be offered CR, despite TS having a similar in-hospital mortality to ACS. Many women with TS experience ongoing symptoms of chest pain, dyspnea and debilitating fatigue that impacts upon their quality of life and increases levels of stress and anxiety.
- Some elements of CR are likely to be useful in aiding recovery from TS. These include addressing knowledge gaps through informing patients about the disease process, what to expect in terms of recovery, and what to do in case of ongoing symptoms or recurrence of TS. Advice on safe use of new medication and stress reduction is also important for women with TS.
- Nurses working in inpatient and primary care community clinics can take practical steps to inform and support women with TS, but to be effective, nurses themselves need to have a good understanding of the condition and the health needs of women with TS.

CONCLUSION

Compared with women with TS, women with ACS in this study were significantly more likely to have been referred to CR and more likely to attend an outpatient CR program to receive educational support, particularly following hospital discharge. The majority of women with TS were not routinely exposed to educational support about how to manage new medications, what to expect in terms of recovery from TS, and what to do in case of ongoing symptoms or recurrence.

Consistent with findings from recent studies, the current study found that women with TS had very little access to support or information about TS, particularly following hospital discharge. Although stress and anxiety are prevalent in women with TS and are known triggers for TS, women with TS in this study were far less likely to receive advice or counseling in management of stress than those with ACS. There may be a role for CR that is tailored to the educational and support needs of women with TS with the aims of promoting recovery and improving quality of life and wellbeing.

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DECLARATION OF CONFLICTING INTERESTS

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