CHAPTER V: DISCUSSION

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5.1. Outline

Cardiac Rehabilitation had been conceived as a part of treatment for patients who had suffered from MI in mid 60s and till now, the benefits of exercise training as a part of cardiac rehabilitation have been well established in many published researches and studies. However enough number of evidence showed that exercise based cardiac rehabilitation in post MI and revascularization patients reduces all-cause mortality by at least 25 to 31%, but still reports from different countries shows only a 25-30% of adherence rate in these programs. The 1995 cardiac rehabilitation clinical practice guideline documented that a less number of patients who are appropriate for cardiac rehabilitation services were referred and enrolled. Over a decade later, the use of cardiac rehabilitation services by Medicare beneficiaries after MI or CABG remains low. Furthermore, enrollment in cardiac rehabilitation varies dramatically by US states & regions and women & elderly patient’s remains less likely to participate. However the role of cardiac rehabilitation having been extensively documented, endorsed and promoted by statements for the comprehensive secondary prevention of cardiovascular events, performance measures for referral to and delivery of the vastly underutilized cardiac rehabilitation services were not available until 2007 in US. These performance measures were created for hospital settings, office practices and cardiac rehabilitation centers, designed as a mechanism to more rapidly translate the strongest clinical evidence into practice and providing incentive for rehabilitation referral and better standardization of care.

Many researches and evidence agree with some common barriers and difficulties with standard Hospital-based cardiac rehabilitation like inconvenient scheduling, lack of transportation, financial burden and insurance problems, far distances of the center, strength of physician recommendation, poor organization of the programs, belief and information of patient about the disease and its management.

Barriers and difficulties of Hospital based cardiac rehabilitation programs lead to design and practice of new alternatives like Home-based
cardiac rehabilitation programs with potential to increase participation rate by meeting the individual needs of patient.\textsuperscript{21}

Despite the wide range of many studies on cardiac rehabilitation in coronary artery disease patients, its applicability, barriers, alternative methods and protocols and their clinical and functional effectiveness is still under question and the results are diverse. \textsuperscript{(Yates\textsuperscript{91} et. al. 2007\textsuperscript{91}, Taylor\textsuperscript{92} et al. 2006, Collines\textsuperscript{93} et al.2001).} Many researchers and clinicians in previous original studies as well as meta-analysis \textsuperscript{(Blair\textsuperscript{109} et al. 2010, Jolly\textsuperscript{98} et al. 2006, Papadakis\textsuperscript{94} 2005)} highlighted the need of more diverse research on the same for more uniform of Home-based programs. Two more recently important published meta-analysis \textsuperscript{(Blair\textsuperscript{110} et al. 2011, Dalal\textsuperscript{111} et al. 2010)} still reflects a heterogeneity in center based cardiac rehabilitation interventions, differences in recruitments and variation in outcomes across studies and need for further research. In addition, reports from different countries and organizations (AACVPR CR resource Manual) also show a diversity of methods and protocols and different outcomes which are not uniform in researches.

In developing countries like India & Iran, practical picture as well as research aspect of cardiac rehabilitation is more vague and much more underutilized than developed countries. In India, in spite of huge population which is going to face 111% increase in cardiovascular disease death till 2020 (Rajasekhar\textsuperscript{5} 2004), there are only very less numbers of cardiac rehabilitation centers which is only available in few large cities. Considering that 70 % of population in India live in rural areas\textsuperscript{112} (considering minimum of 5000 people as Urban area\textsuperscript{113}) and even reaching to regular hospitals are difficult for them, one could imagine the huge difference and gap in practice of cardiac rehabilitation, health care and quality life of cardiac patients in this country.

Iran, a developing country with some common cultural issues with India and some differences is another example of underutilization of cardiac rehabilitation. Unlike India 70% of population of Iran live in urban areas\textsuperscript{112} (considering minimum of 5000 people as urban area\textsuperscript{113}) and there is a good access to large cities by roads and good transport system. But there are very few centers which provide cardiac rehabilitation services and only restricted to
Tehran and few large cities. One of the major aspects of underutilization of cardiac rehabilitation in Iran is lack of insurance support and Medicare for coverage of Rehabilitation expenses and poor referral and belief from cardiologists.

Therefore we undertook this study to compare Hospital-based versus Home-based cardiac rehabilitation in low and moderate risk coronary artery disease patients and to find out its effectiveness in clinical outcomes like Left Ventricular Ejection Fraction, Functional capacity and Quality of life in India and Iran with two different population and set up. This will increase the generalizability of results and recruiting more variety of patients with hope to put light in the current status of cardiac rehabilitation globally as well as in our population.

In first time interval of our study, from April 2008 to May 2009 we enrolled and completed 60 subjects in center 1, Kasturba Hospital, Manipal. In 2nd interval, from June 2009 to February 2010 we continued enrolling patients from second center, Golsar Hospital, Iran, and 43 subjects enrolled and completed the study. And in third interval, from March 2010 to November 2010 again we continued enrolling the remaining of 77 subjects in Kasturba Hospital, Manipal.

Kasturba Hospital is located in Manipal town which belongs to Udupi District at Karnataka state of India. The three northern taluks, Udupi, Kundapur and Karkala, are separated from Dakshina Kannada District to form Udupi district. Udupi district is surrounded by Uttara Kannada district in north, Dakshina Kannada district in southern direction. Shivamogga district borders on north east side and chikamagalur district on east. Arabian Sea is on west of Udupi district. The administrative headquarters of Udupi district is Udupi town. Population as per Census 2001 was 1,112,243 of which 18.55% were urban. Udupi taluk is a taluk in the Udupi District of the Indian state of Karnataka. The headquarters is the town of Udupi. There are 99 villages identified as part of Udupi taluk.\textsuperscript{114,115}
Golsar Hospital is located in Rasht (شت) city, the capital of Guilan province in North Western Iran and the largest city along the Caspian Sea coast. Rasht is also a major tourist center with the resort of Masouleh in the adjacent mountains and the beaches of Caspian Sea as some of the major attractions. Rasht had an estimated population of 560,123 in 2005.

In the present study, overall we screened 660 post-coronary event patients (their first episode) who were treated surgically or conservatively for the eligibility criteria to enrol in the study. Out of 660 subjects, 480 subjects excluded (did not meet inclusion criteria or refused to participate in the study). Thus, as per the sample size calculation total of 180 patients who met inclusion criteria who given written informed consent enrolled in the study and randomized (block size of 6) into three groups (60 in each group) of Hospital-based, Home-based cardiac rehabilitation and control group. Total of 15 subjects lost to follow up (2 in Hospital based, 5 in Home based and 8 in control group) and one subject from control group expired due to Post CABG re-admission and respiratory complications.

Mean age of subjects was 57.7± 9.3 years; however there was no significant difference between groups with respect to age. Male to female ratio was 146/34; however there was no significant difference between groups with respect to gender distribution. 49.4 % of subjects were low risk and 50.6% were moderate risk and there was no significant difference between groups with respect to their risk stratification level. (Tables 4.1 to 4.3, and Figures 4.2 to 4.9)

Analysis and discussion of the results are summarized based on the primary outcomes including Quality of life, LVEF, and functional capacity in the following sections.
5.2. Study on Quality of Life

A benchmark meta-analysis by Jolly et al. (2006) reported that available data shows a mix report on the effectiveness of Home-based cardiac rehabilitation programs on quality of life, its acceptability and cost-effectiveness and debate has to continue by further studies for more accurate results.

Karapolat et al (2007) reported a better quality of life outcome in hospital-based supervised exercise training compared to home-based training program in heart transplant subjects.101

A recently published review by Blaire (2010-2011) still highlighted that because of great heterogeneity between study populations, lack of standardization of entry criteria to cardiac rehabilitation programs, and the exact details of Home-based programs and its variety makes direct comparison of studies and drawing a firm conclusion difficult.109,110

From our study we found a significant difference between Hospital based-group and Control (p<0.0001) as well as Home-based group in comparison with Control group (p<0.0001) in both Physical Composite Score (PCS) and Mental Composite Score (MCS) of SF-36 v2. (Table 4.4, Figures 4.10, 4.11 & 4.12) However, pairwise comparison by Tuckey HSD revealed no significant difference between Hospital-based and Home-based groups in PCS component (p=0.94) as well as MCS component (p=.94) (Table 4.4, Figures 4.10, 4.11 & 4.12)

These findings are in accordance with Schmid et al.(2010), Arthur et al. (2001) & Lavie et al. (2000).

In analysis of each 8 subdomains of SF-36V2, we found significant improvement in all subdomains following 12 weeks cardiac rehabilitation in both Hospital-based and home-based groups compared to control group. (Table 4.21, Figure 4.45) But post hoc pairwise comparison by Tuckey HSD showed no significant difference between Hospital-based and Home-based groups in all subdomains. Thus, our findings showed Home-based programs could be as
effective as Hospital-based programs in improving the quality of life of patients following coronary event.

Our findings are in consistent with a recently published and large meta-analysis by Dalal\textsuperscript{111} et al. (2010) in which found an equal improvement in Health related quality of Life outcomes in Hospital based and Home-based cardiac rehabilitation programs. But they mentioned that their study had limitation due to heterogeneity for several outcomes across the trials including variety of center-based interventions, differences in recruitment and characteristics of patients.

Our findings are also in consistence with overall other reports from Ashworth\textsuperscript{102} et al (2005), Marchionni\textsuperscript{26} et al. (2003) and Arthur\textsuperscript{24} et al. (2002), however they reported the overall scores of outcomes and details of the subdomains were not clear.

Center-wise analysis of SF-36 revealed almost a similar result. In both centers there was a significant improvement in quality of life, Physical Composite Score and Mental Composite Score of patient in both Hospital & Home-based groups compared with Control. But there was no significant difference between Hospital & Home-based group.

In analysis of subdomains of SF36, our result showed a significant improvement in all subdomains in both Hospital & Home-based group. (Tables 4.13, 4.21, Figures 4.30, 4.44) this could be a possible reason that improvements in all subdomains of SF36 like Physical function, Role physical, Body pain, Vitality, Social function, Role emotional & Mental health lead to improvements of QOL of patient. But there was no significant difference between Hospital & Home-based groups. (Figures 4.30, 4.44)

By looking at details of changes in subdomains of SF36, results of present study showed the maximum improvement among subdomains was related to SF (Social Function) & RP (Role Physical) subdomains. Center-wise analysis showed similar result. (Figures 4.13, 4.30, and 4.44)
5.3. Study on Left Ventricular Ejection Fraction (LVEF)

However Left ventricular ejection fraction is a major and practical clinical outcome for evaluating myocardial contractility and its pumping action\textsuperscript{15, 16} and is a well-established predictor of mortality and long term prognosis in Coronary artery disease patients but it has not been much studied as an outcome in cardiac rehabilitation programs and related research. Previous published studies mainly studied this outcome in heart failure patients or they used a heterogeneous subject groups with respect to the time gap between coronary event and start of exercise training or total duration of the program.

In the present study we studied and compared the effect of Hospital-based versus Home-based exercise based cardiac rehabilitation on LVEF and compared it with control group with no rehabilitation. Our results revealed a significant improvement in LVEF after 12 weeks in both Hospital-based (p<0.0001) and Home-based (p<0.0001) cardiac rehabilitation groups compared to Control group. There was also a significant difference between Hospital-based and Home-based group in favor of Hospital-based group.(p=0.001) (Table 4.6, Figure 4.14)

This finding is in accordance to results from Adachi\textsuperscript{42} et al. (1996) in which reported improvement in cardiac function (such as stroke volume), both at rest and during exercise only with high intensity exercise training.

Possible mechanism behind this could be the compensation strategy by the non-infarcted region or the effect of exercise on collateralization of coronary arteries and improvement in myocardial function. Giallauria\textsuperscript{119} et al. (2008), also found a favorable remodeling from six months exercise training program in patients with moderate left ventricular dysfunction\textsuperscript{24} Schmid\textsuperscript{120} et al. (2010) in his recently published paper, explained about mechanism of reverse remodeling following exercise training and improvement in LVEF in heart failure patients.

However our findings are in contrast with report from Cobb\textsuperscript{121} et al. (1982), in which they found no changes in LVEF after 6 months of exercise training in post-MI patients. But their study was seeking from a small sample size of 15
subjects and a very heterogeneous type of patients in terms of time gap between MI and start of exercise training which was varied from 6 weeks to 6 months.

Our findings are in parallel with a recently published paper by Schmid et al. (2010) where in reported a significant improvement in LVEF after 3 months cardiac rehabilitation. However target population in his study was heart failure patients.\textsuperscript{120}

Our findings showed that a structured individually tailored Home-based cardiac rehabilitation could significantly improve LVEF, and could be safe to use in moderate risk coronary artery disease patients, however in comparison with Hospital-based program the percentage of change is significantly less. (p=0.001) (Table 4.6, Figure 4.14)

Sub-analysis of our results with respect to each center showed a significant difference between both Hospital-based and Home-based compared with Control as well as a significant difference between Hospital & Home-based groups in improving LVEF in center I in India (Table 4.14, Figure 4.31). On the other hand, in Center II in Iran, however there was significant difference in both Hospital and Home-based groups compared with Control but there was no significant difference between Hospital & Home-based groups (p=0.8) (Table 4.22, Figure 4.45)

By looking at the characteristics of patients closely in two centers, we found that there was a difference between two centers with respect to risk level; 53.3% moderate risk in center I compared to 81.4% in center II. Risk level of patient which was determined based on baseline EF, functional capacity of patient could be a possible reason for this difference. This finding is in accordance with findings of Giuseppe Specchia\textsuperscript{122} (1996).
5.4. Study on Functional Capacity

In the present study, results revealed a significant improvement in functional capacity after 12 weeks cardiac rehabilitation in both Hospital-based (p<0.0001) and Home-based group (p<0.0001) compared to Control group.

In different studies from small sample studies (Cobb et al, 1982)\textsuperscript{121} to larger ones (Arthur et al, 2002)\textsuperscript{24}, and in spite of a huge heterogeneity in terms of type of exercise, type of test, type of patients between many researches, but majority of them reported a significant improvement in functional capacity and exercise tolerance after exercise based cardiac rehabilitation, and our result is comparable to them. Few large scale systematic reviews and meta-analysis (Blair\textsuperscript{109} 2010, Wegner\textsuperscript{108} 2008, Jolly\textsuperscript{98} 2006) also had similar reports while comparing Home-based and center based cardiac rehabilitation programs.

In our study, post hoc pairwise comparison by Tuckey HSD also showed a significant difference between Hospital-based and Home-based group (p<0.0001) in favor of hospital-based group. (Table 4.7, Figure 4.15)

Dutcher, Kahn, Grines et al and Franklin (2007) reported that exercise capacity and Left ventricular ejection fraction (LVEF) are predictors of long-term mortality in post-MI patients but MET level is a stronger predictor than LVEF.\textsuperscript{99} This, shows the importance of functional capacity as a stronger outcome for evaluating patient and monitor the progress of patient.

According to our findings Home-based cardiac rehabilitation could significantly improve functional capacity however, in comparison with Hospital based group the amount of change is significantly less. (p<0.0001) (Figure 4.15)

Center-wise analysis of functional capacity showed that similarly in both centers there was a significant improvement in functional capacity in both Hospital & Home-based groups compared with Control group. But in both centers there was no significant difference between Hospital & Home-based group. (Figures 4.29, 4.44) Since the result of pooled data from both centers for complete sample size showed a significant difference between Hospital &
Home-based group (p<0.0001), this difference in result of center-wise analysis versus pooled data could be simply attenuated because of using fraction of whole sample size.

5.5. Study on secondary outcomes

Analysis of our data on secondary outcomes including BMI, waist circumference and three points skinfolds measurement showed a significant reduction in BMI and skinfolds measurements in both Hospital-based and Home-based groups compared to control group. But there was no significant difference between Hospital-based and Home-based programs. There was no significant difference in Waist circumference among the three groups. (p=0.09) (Table 4.8, Figures 4.16 to 4.18)

5.6. Drop out & Adherence

However in the planning phase of study, based on previous studies we considered 25 % drop out in sample size calculation, but the actual drop out rate in present study was 8.3 % (15/180). [Figure 4.1] And one subject in Control group expired due to pulmonary infections and post-CABG complications. Other studies and available recent evidence reported a 20% to 40 % drop outs \(^{24}\) (Barbour\(^{123}\) 2008, Wenger\(^{108}\) et al. 2008, Arthur\(^{24}\) et al. 2002) which is much higher than our results. Center-wise comparison also showed 8.0 % (11/137) in Center I, in India and 9.3 % (4/43) in center II in Iran. (Figures 4.19 & 4.34)

Results of present study showed 53.3% of total drop outs belonged to Control group whom did not receive any rehabilitation program. Home-based group had about 33.3 % of total drop outs and Hospital-based had the least percentage of only 13% (2/15) of total drop outs (Figure 4.1)

A possible reason for overall less drop outs in present study could be higher motivation of patients due to educational program, regular follow ups and phone contacts by research scholar. In addition to Reimbursement of expenses to all 3 groups, Hospital-based group received Transport expenses to attend the program at center which could be a possible reason for less dropout rate in Hospital-based group. Certainly this facility played an important role to reduce the drop outs in our study.
Our finding is in consistence with recent unpublished results from Babu et al. wherein found a 9.7 % drop out in their Home-based cardiac rehabilitation program.\textsuperscript{124}

Adherence rate in experimental groups in the present study in Hospital-based group was less compared to Home-based programs. We found that median number of days which patients attended Hospital-based program was 25 sessions out of 36 (12 weeks x 3 session/week) and for Home-based group was 32 sessions out of 36. A possible reason for more adherence rate in Home-based group could be in Home-based group, patients had freedom to select their exercise time according to their convenience performed the suggested exercise more number of days as suggested to them compared to Hospital-based group.

In summary, results of present study showed that regular follow up through telephone calls at 2 weeks intervals and every month supervision in Home-based group, and regular attendance in the Hospital-based group in the present study was a successful model to reduce drop outs; in fact highest drop out rates in present study belonged to Control group whom did not receive any type of rehabilitation or education about these programs and its importance. Thus, it seems in developing countries like India & Iran, education of patients and explaining the importance of concept of cardiac rehabilitation, its role in the management of CAD could encourage the post-coronary event patients to attend cardiac rehabilitation programs either in the form of Hospital or Home-based programs.

5.7. Limitations of study

A major limitation of present study was limited fund and time duration to spend in the center in Iran. Research scholar had only 6 months’ time to recruit patients in Iran which was not possible to recruit equal number of patients as in India. Thus, making accurate comparison of results between two countries was limited.

Another limitation in present study was unavailability of community-based facilities and a special team to help the researcher to reach at patient’s
destination and supervise the exercise performance in Home-based group. Availability of the same could have made the Home-based programs more efficient.

5.8. Clinical Implication

From our study, it was concluded that Cardiac rehabilitation program is effective for our population in developing countries. Strategies like Home-based programs has the potential to be as effective as Hospital-based program and to be more accessible and cost effective for patient with CAD to be benefited by the program and could become a part of cardiac care in our population. It could reduce the morbidity and improve the quality of life of patients and also it could reduce the financial burden imposed on patients in developing countries like India & Iran.

5.9. Suggestion for future research

Future research could be directed for longer term (3 month to one year) monitoring and follow up of patients and to find out the adherence rate in our population, and comparing the results with other countries could provide us vital knowledge to help to overcome the gap between practice and research in our population.

However our study focused on Low & moderate risk CAD patients, future research could be directed to establish a safe Home-based program for High risk group of patients and compare its efficacy on clinical as well as QOL outcomes. Certainly such research will provide appropriate cardiac care for the common man who reside in rural areas and do not have access to advanced centers.