

Results

Baseline characteristics:

One hundred and seventy patients were included from Mar. 2011 to September 2011 (mean age 68.8 ± 9.7 years, 38 females and 132 males). Ninety-one patients had non-ischemic cardiomyopathy (NICM) and 79 patients had ischemic cardiomyopathy (ICM), of whom 43 patients had previous myocardial infarction. Most patients with ICM underwent previous revascularization (60 patients underwent previous revascularization). Table 3.1, 3.2 and 3.3 summarize the baseline data of our patients.

| Baseline condition | Mean/n(%) |
|------------------------------------|------------------|
| Age, years | 68.8 \pm 9.7 |
| Male/female ,n | 132/38 |
| NYHA II ,n | 23 (13.5%) |
| NYHA III ,n | 136 (80%) |
| Ambulatory NYHA IV ,n | 11 (6.5%) |
| 6 min walk distance, m | 275 \pm 105 |
| NICM, n | 91(53.5%) |
| ICM, n | 79 (46.5%) |
| Previous MI, n | 43 (25.3%) |
| Previous revascularization, n | 60 (35.3%) |
| BMI , Kg/m ² | 29.2 \pm 5.1 |
| Use of medications (% of patients) | |
| B blockers | 94% |
| ACEi/ARB | 95% |
| MRA ^a | 64% |
| Diuretics | 92% |
| Statins | 69% |
| Digoxin | 41% |
| Antiarrhythmic drugs, % | 29% |
| Comorbidities | |
| Hypertension , n | 139 (81.7%) |
| DM, n | 86 (50.5%) |
| COPD ^b , n | 44(25.8%) |
| BMI>30, n | 55 (32.3%) |
| History of renal disease, n | 56 (32.9%) |
| Anemia ^c , n | 102 (60%) |
| S. Creatinine, mg/dl | 1.2 \pm 0.4 |
| Blood urea nitrogen, mg/dl | 9.5 \pm 6.4 |
| eGFR, ml/min/1.73m ² | 53.7 \pm 10.3 |
| Hb level, gm/dl | 9.9 \pm 7.1 |

| | |
|----------------------|--------|
| Blood Glucose, mg/dl | 136±59 |
|----------------------|--------|

Table 3.1: Baseline characteristics; clinical data

^aMRA: Mineralocorticoid Receptor Antagonists ^bCOPD: Chronic obstructive pulmonary disease (based on specialized respiratory assessment and use of specific medications). ^cAnemia (defined as hemoglobin (Hb) level < 11g/dl).

| Baseline ECG | Mean/n(%) |
|-------------------------------------|-------------|
| QRS duration | |
| Mean , msec | 145±25 |
| ≥120 msec | 145 (85.3%) |
| ≥150 msec | 89 (52.3%) |
| ≤120 msec | 25 (14.7%) |
| QRS morphology | |
| LBBB | 94 (55.3%) |
| RBBB | 4 (2.3%) |
| IVCD ^a | 47 (27.6) |
| Normal | 25 (14.7%) |
| Rhythm | |
| History of AF | 51(30%) |
| SR at CRT implantation | 147 (86.5%) |
| AF at CRT implantation ^b | 32 (13.5%) |

Table 3.2: Baseline characteristics; ECG

^aIVCD: Intraventricular conduction delay. ^bAV nodal ablation was done in 8 patients

| Baseline echocardiography | Mean/n(%) |
|-------------------------------|-------------|
| LV dimensions, volumes and EF | |
| LVIDd (mm) | 67.58±9.2 |
| LVIDs (mm) | 55.71±10.3 |
| LVEDV (ml) | 205.72±66.4 |
| LVESV (ml) | 148.30±56 |
| LVEF % | 28.31±7.2% |
| Mitral regurgitation | |
| No/mild | 114 (67%) |
| Moderate | 41(24%) |
| Severe | 15 (9%) |
| Diastolic dysfunction | |
| No/grade I | 51 (35%) |
| Grade II | 53 (36%) |
| Grade III | 43 (29%) |
| Right ventricle | |
| TAPSE (mm) | 18.16±3.8 |
| RVd (mm) | 34.15±5.9 |
| No PHT | 51 (30%) |

| | |
|--------------------------------|-------------|
| PAP 35-50 mmhg | 76 (44.7%) |
| PAP >50 mmhg | 43 (25.3%) |
| Markers of dyssynchrony | |
| SPWMD (msec) | 120.73±63.3 |
| FT/RR % | 37.64±8.3% |
| LVPEI (msec) | 128.50±30.4 |
| IVD (msec) | 39.28±25.9 |
| Ts- sep-lat (msec) | 63.22±34.7 |

Table 3.3: Baseline characteristics; echocardiography

CRT implantation Procedure:

CRT-P was implanted in 65 patients and CRT-D was implanted in 105 patients. The right atrial lead was inserted in the right atrial appendage in all cases. The right ventricular lead was inserted at the right ventricular apex in all cases. The left ventricular lead position was assessed in LAO and RAO views to assess its short axis and long axis position (figure 3.1). The position of the LV lead was based on the anatomy of the coronary sinus. The lateral, posterolateral and posterior position were considered optimal short axis positions. long axis positions other than apical were considered optimal. The LV lead position was considered to be optimal when it is optimal in both long axis and short axis (table 3.4).

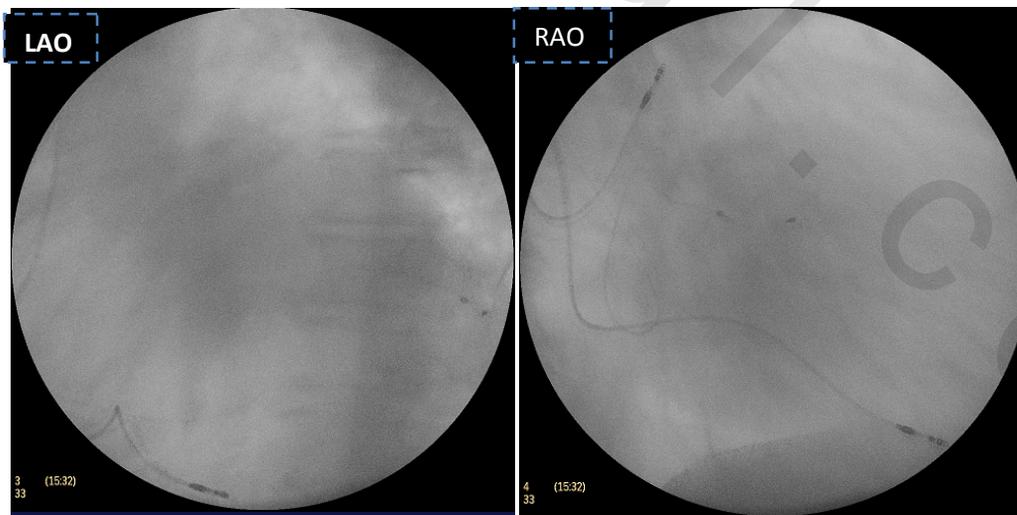


Figure 3.1: Example LV lead position in basal lateral wall.

| LV lead short axis position | n (%) |
|-----------------------------|------------|
| Lateral | 52 (30.6%) |
| Posterolateral | 69 (40.5) |

| | |
|-----------------------------|-------------|
| Posterior | 39 (22.9) |
| Anterolateral | 7 (4%) |
| Anterior | 3 (1.8%) |
| Optimal short axis position | 160 (94.1%) |
| LV lead long axis position | |
| Basal | 17 (10%) |
| midwall | 144 (84.7%) |
| Apical | 9 (5.3%) |
| Optimal long axis position | 161(94.7%) |
| Optimal LV lead position | 153 (90%) |

Table 3.4: LV lead position

Device optimization using device based automated algorithms was performed at the same implantation day in 57.6% of patients. Biventricular pacing percent was $96 \pm 7\%$ at 1 day post-implantation and was $95 \pm 7\%$ at 6 months post-implantation. Device optimization was done again at 6 months for the nonresponders.

CRT response:

Among the study population, 114 patients (67.1%) responded to CRT implantation (defined as improvement of NYHA functional class by ≥ 1 NYHA class, increased 6.MWD $\geq 10\%$ and reduction of LVESV $\geq 15\%$ at 6 months after CRT implantation), 56 patients didn't respond. Improvement of NYHA class was maintained 1 year after CRT implantation. Mortalities and hospitalization related to unprovoked worsening of heart failure during the 1st 6 months postimplantation was considered CRT-nonresponse.

At 6 months follow-up, CRT implantation was associated with significant improvement in LV dimensions, functions and markers of LV dyssynchrony. CRT implantation was associated with improvement in NYHA class and 6 min walk distance. CRT was also associated with significant improvement in LV diastolic dysfunction and the grade of mitral regurgitation. There were no significant effects on renal function and RV diastolic dimension and function. Tables 3.5 and 3.6 summarize different effects of CRT implantation.

| Parameter | Baseline (n=170) | 6 months (n=170) | P |
|------------|------------------|------------------|-------|
| LVIDd (mm) | 67.91 ± 8.7 | 64.95 ± 8.9 | 0.001 |

| | | | |
|----------------------------------|-------------|-------------|--------|
| LVIDs (mm) | 57.02±8.8 | 52.42±9.9 | 0.0001 |
| LVEDV (ml) | 208.39±69.1 | 185.46±61.3 | 0.0001 |
| LVESV (ml) | 150.50±58.6 | 121.57±55.4 | 0.0001 |
| LVEF % | 28.38±7.2% | 35.46±9.3% | 0.0001 |
| Grade of Mitral regurgitation | 1.46±0.7 | 1.21±0.7 | 0.032 |
| Grade of diastolic dysfunction | 1.89±0.8 | 1.54±0.8 | 0.026 |
| TAPSE (mm) | 18.27±4.2 | 18.55±4.3 | 0.535 |
| RVd (mm) | 33.77±4.8 | 34.55±4.7 | 0.118 |
| Grade of tricuspid regurgitation | 1.07±0.7 | 1.07±0.7 | 1.0 |
| SPWMD (msec) | 144±86.4 | 31.33±43.7 | 0.0001 |
| FT/RR % | 35.71±9.1% | 44.71±5.6% | 0.004 |
| LVPEI (msec) | 124.79±20.1 | 110.57±33.2 | 0.059 |
| IVD (msec) | 23.83±26.6 | 15.83±13.3 | 0.375 |
| Ts- sep-lat (msec) | 67.69±36.6 | 35.38±19.4 | 0.007 |

Table 3.5: Effects of CRT; echocardiography

| Parameter | Baseline n=170 | 6 months n=170 | P |
|--------------------------------|-------------------|-------------------|--------|
| NYHA class | 2.91±0.4 | 2.18±0.6 | 0.0001 |
| 6 min walk distance (m) | 275±105 | 414±111 | 0.001 |
| Creatinine mg/dl | 1.27±0.4 | 1.3±0.6 | 0.245 |
| B urea Nitrogen mg/dl | 10.7±7.8 | 9.8±4.8 | 0.318 |
| eGFR ml/min/1.73m ² | 53±10.6 | 52.3±13.1 | 0.589 |

Table 3.6: Effect of CRT on clinical status and renal function

Clinical events:

There were 27 heart failure related hospitalizations. The rehospitalization rate was significantly higher among nonresponders compared to the responders (19 (33.9%) vs 8 (7%), P= 0.00001). There were also 15 heart failure related mortalities (11 (19.6%) nonresponder vs 4(3.5%) responders, P=0.0001).

Differences between responders and nonresponders:

Compared to nonresponders, responders had significantly wider baseline QRS duration, lower BMI, lower baseline serum creatinine level, smaller baseline RV diastolic dimension and greater TAPSE value. There was a significant gender difference between responders and nonresponders. Responders were less likely to have PAP>50 mmhg at baseline, less likely to have grade III diastolic dysfunction, more likely to have NICM, more likely to have LBBB morphology in ECG, less likely to have AF at implantation time, less likely to have history of renal disease and less likely to have COPD than nonresponders.

There were no baseline differences in the presence and severity of mitral regurgitation. Baseline NYHA functional class was not different between responders and nonresponders. There were no significant differences in age, BUN, eGFR, blood glucose, hemoglobin level, BiV pacing percent, baseline left ventricular dimensions, volumes, ejection fraction and the measured echocardiographic parameters of LV dyssynchrony between responders and nonresponders. Table 3.7, 3.8 summarize the baseline differences between responders and nonresponders.

| Parameter | Responder n = 114 Mean | Nonresponder n= 56 Mean | P |
|-----------------------------------|------------------------------|-------------------------------|--------|
| Age (years) | 68.8±10.3 | 68.9±8.2 | 0.9 |
| BMI (kg/m ²) | 28.6±4.7 | 30.4±5.5 | 0.04 |
| Creatinine (mg/dl) | 1.17±0.4 | 1.35±0.4 | 0.007 |
| B. urea nitrogen (mg/dl) | 9.2±6.5 | 10.2±6.2 | 0.3 |
| eGFR (ml/min/1.73m ²) | 54.5±9.6 | 52.4±11.5 | 0.25 |
| Bl. Glucose (mg/dl) | 131±48. | 149±62 | 0.07 |
| Hb level (gm/dl) | 10.3±8.7 | 9.3±1.3 | 0.2 |
| QRS duration (msec) | 152±24.9 | 130.7±24 | 0.0001 |
| BiV pacing% | 95±4 | 94±4 | 0.7 |
| LVIDd ;mm | 67.7±8.9 | 67.3±9.8 | 0.8 |
| LVIDs ; mm | 55.4±10.2 | 56.3±10.6 | 0.6 |
| LVEDV ; ml | 205.7±66.3 | 205.6±67.5 | 0.9 |
| LVESV; ml | 147.7±54.3 | 149.5±60.3 | 0.8 |
| LVEF % | 28.3±6.7% | 28.2±8.2% | 0.9 |
| SPWMD; msec | 126.2±66 | 110±56.9 | 0.09 |
| TAPSE; mm | 18.9±3.7 | 16.6±3.5 | 0.001 |
| RVd; mm | 33±6.3 | 36.3±4.3 | 0.001 |
| FT/RR % | 37.2±7.9% | 38.4±9.2% | 0.4 |
| LVPEI; msec | 131.9±31.2 | 122±28.2 | 0.4 |
| IVD; msec | 40.6±26.8 | 36.3±23.6 | 0.3 |

| | | | |
|------------------|---------|-----------|-----|
| Ts-sep-lat; msec | 66+32.1 | 57.2+39.7 | 0.1 |
|------------------|---------|-----------|-----|

Table 3.6: Responders vs. nonresponders baseline characteristics

| Parameter | Responders n= 114 | Nonresponders n=56 | P value |
|--|----------------------|-----------------------|---------|
| Females | 33 (28.9%) | 5(8.9%) | 0.002 |
| NICM | 73 (64%) | 18 (32.1%) | 0.0001 |
| LBBB | 78 (68.4%) | 16 (28.6%) | 0.00001 |
| AF at implantation | 8 (7%) | 15 (26.8%) | 0.001 |
| History of renal disease | 26 (22.8%) | 30 (53.6%) | 0.0001 |
| COPD | 21 (18.4%) | 23 (41.1%) | 0.002 |
| Grade III diastolic dysfunction | 17 (14.9%) | 16 (28.6%) | 0.034 |
| PAP>50 mmhg | 18 (15.8%) | 17 (30.4%) | 0.027 |
| HF hospitalizations | 19 (33.9%) | 8 (7%) | 0.00001 |
| HF mortalities | 11 (19.6%) | 4 (3.5) | 0.0001 |

Table 3.7: Responders vs. nonresponders baseline characteristic and events.

Predictors of CRT response:

Gender:

Females have been more likely to respond to CRT than males (84% vs. 61% respectively, P=0.003). This difference was not significant in multinominal regression analysis (OR 3.3; 95% CI 0.8-13.2, P= 0.09).

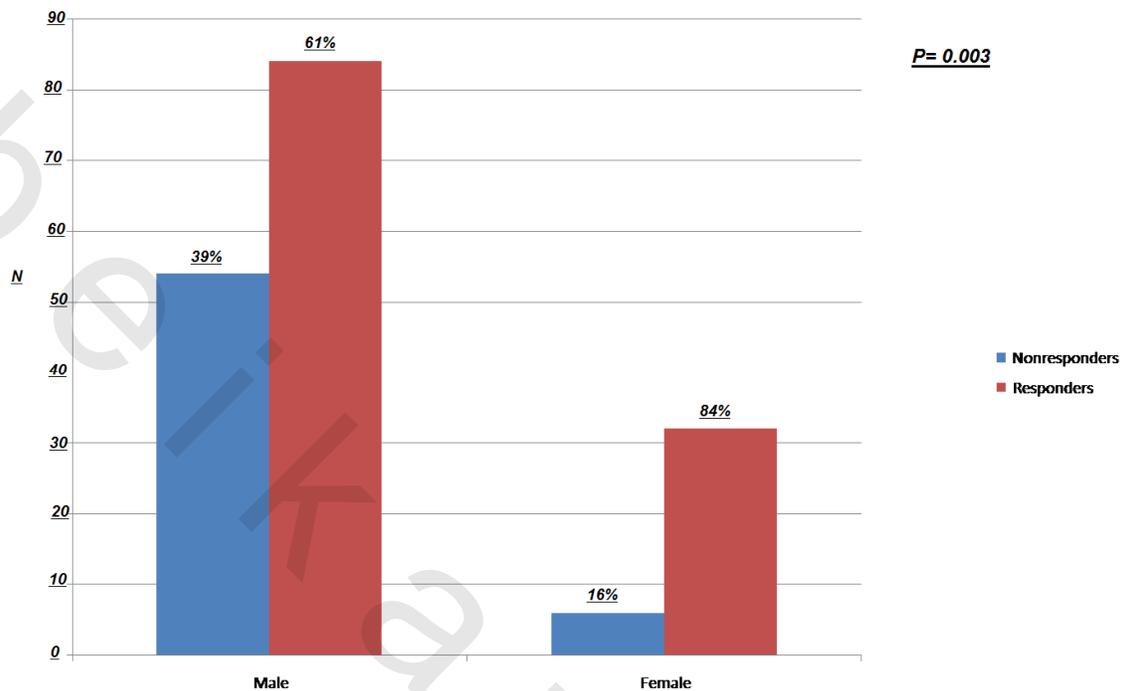


Figure 3.6: Gender difference in response

Baseline NYHA class and response:

Patients with NYHA class II and III at baseline did well after CRT implantation (response rate 69.6 and 68.4 respectively). The response rate in patients with baseline ambulatory NYHA IV was worse than other patients (45.5% response rate), but was not statistically significant due to small number of patients in NYHA IV included (11 patients).

| Baseline NYHA | Nonresponders n=56 | Responders n= 114 | P |
|---------------|-----------------------|----------------------|-------|
| NYHA II | 7 (30.4%) | 16 (69.6%) | 0.278 |
| NYHA III | 43 (31.6%) | 93 (68.4%) | |
| NYHA VI | 6 (54.5%) | 5 (45.5%) | |

Table 3.9: Baseline NYHA and response

Comorbid conditions:

The presence of lung disease in the form of significant chronic obstructive pulmonary disease (COPD) was an independent predictor of nonresponse to CRT (OR 0.26; 95%CI 0.08-0.8, P=0.022). The CRT response rate in patients with COPD was 47.7% vs. 73.8% response rate in patient without COPD, P= 0.002. History of renal disease was also an independent predictor of nonresponse (OR 0.14; 95% CI 0.04-0.44, P= 0.001). The responders had significantly lower baseline serum creatinine level. However there were no significant differences in CRT response between patients with eGFR above or below 60 ml/min/1.73m². There was a non-significant trend that non-hypertensive respond to CRT better than hypertensive and non-diabetic patients respond to CRT better than diabetic patients. The CRT response rate didn't differ significantly between obese and non-obese patients.

| Comorbidity | | Nonresponders n=56 | Responders n= 114 | P |
|---------------|--------------------------------|-----------------------|----------------------|--------|
| Lung disease | no COPD | 33 (26.2%) | 93 (73.8%) | 0.002 |
| | COPD | 23 (52.3%) | 21 (47.7%) | |
| Renal disease | no history of renal disease | 26 (22.8%) | 88 (77.2%) | 0.0001 |
| | history of renal disease | 30 (53.6%) | 26 (46.4%) | |
| eGFR | ≥ 60 ml/min/1.73m ² | 25(29.4%) | 60 (70.6%) | 0.09 |
| | < 60 ml/min/1.73m ² | 31(36%) | 54(64%) | |
| Hypertension | No HTN | 6 (19.4%) | 25 (80.6%) | 0.07 |
| | HTN | 50 (36.0%) | 89 (64.0%) | |
| Diabetes | Non-diabetic | 22 (26.2%) | 62 (73.8%) | 0.06 |
| | Diabetic | 34 (39.5%) | 52 (60.5%) | |
| Obesity | BMI <30 | 32 (30.7%) | 71 (69.3%) | 0.378 |
| | BMI ≥30 | 23 (34.4%) | 44 (65.6%) | |

Table 3.10: Co-morbid conditions and CRT response

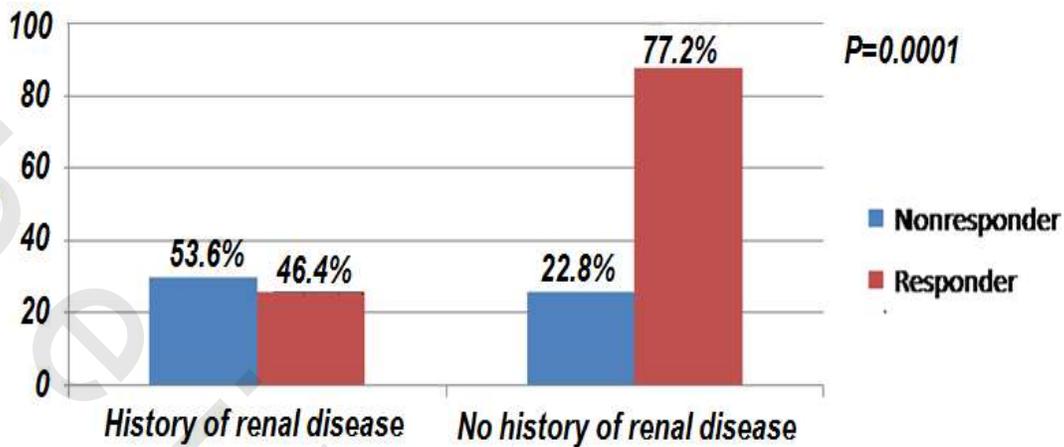


Figure 3.3: Renal disease and CRT response

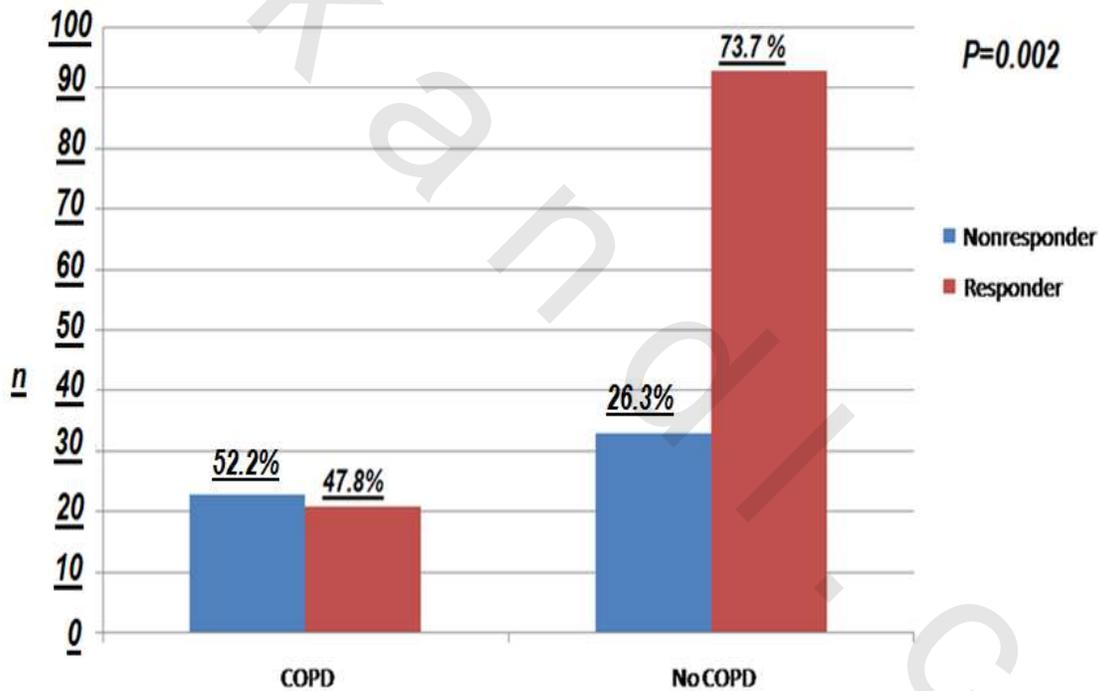


Figure 3.4: COPD and CRT response

ECG:

Patients LBBB were more likely to respond to CRT than patients without LBBB (83% vs. 47.4%, $P=0.0001$). However, LBBB morphology was not an independent predictor of response in multinomial regression (OR 2; 95% CI 0.75-5.4, $P = 0.16$).

QRS duration (QRSd) ≥ 150 msec was the strongest independent pre-implantation predictor of response (OR 9; 95% CI 3.1-27.8, $P < 0.001$). CRT response was documented in 84.5% of patients with baseline QRSd ≥ 150 msec vs. only 50% of those with QRSd < 150 msec, $P < 0.001$. There was no significant difference between patients with $150 > \text{QRSd} \geq 120$ msec and those with QRSd < 120 msec as regards CRT response (52.5% vs. 44% respectively, $P = 0.4$). AF at time of CRT implantation was an independent predictor of nonresponse (OR 0.17; 95% CI 0.04-0.66, $P = 0.01$).

The CRT response rate was much better in patients with SR during CRT implantation than patients with AF (72.1% vs. 34.8% respectively, $P < 0.0001$). There was a significant difference in BiV pacing % between Patients with AF and patients with sinus rhythm at 1 day postimplantation ($91.2 \pm 15\%$ vs. $96.9 \pm 5.7\%$ respectively, $P = 0.001$) and at 3 months postimplantation ($92.4 \pm 10\%$ vs. 96.4 ± 6.8 respectively, $P = 0.01$).

| ECG | | Nonresponders n= 56 | Responders n= 114 | P |
|----------------|-----------------------------|------------------------|----------------------|--------|
| QRS morphology | No LBBB | 40 (52.6%) | 36 (47.4%) | 0.0001 |
| | LBBB | 16 (17.0%) | 78 (83.0%) | |
| QRSd msec | QRS < 120 | 14 (56.0%) | 11 (44.0%) | 0.4 |
| | $120 \leq \text{QRS} < 150$ | 29 (47.5%) | 32 (52.5%) | |
| QRSd msec | QRS ≥ 150 | 13 (15.5%) | 71 (84.5%) | 0.0001 |
| | QRS < 150 | 43 (50%) | 43 (50%) | |
| IO rhythm | SR | 41 (27.9%) | 106 (72.1%) | 0.0001 |
| | AF | 15 (65.2%) | 8 (34.8%) | |

Table 3.11: ECG and response

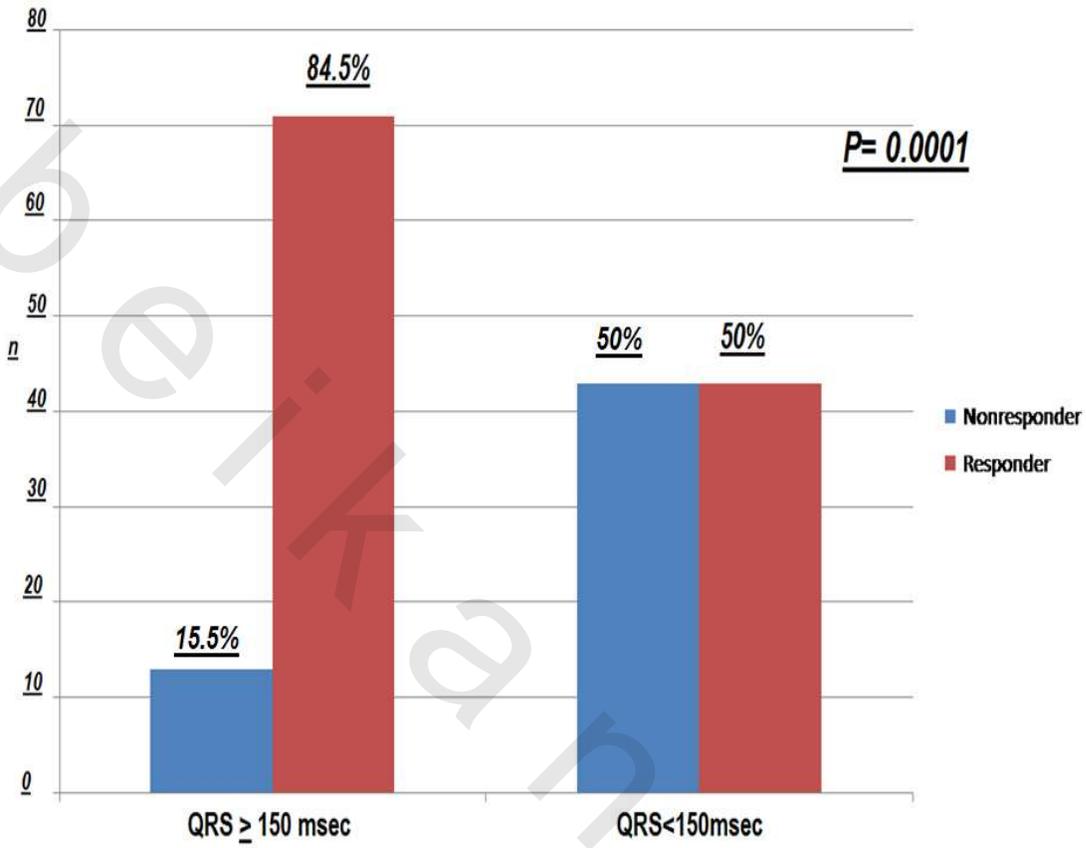


Figure 3.5: QRS duration and response

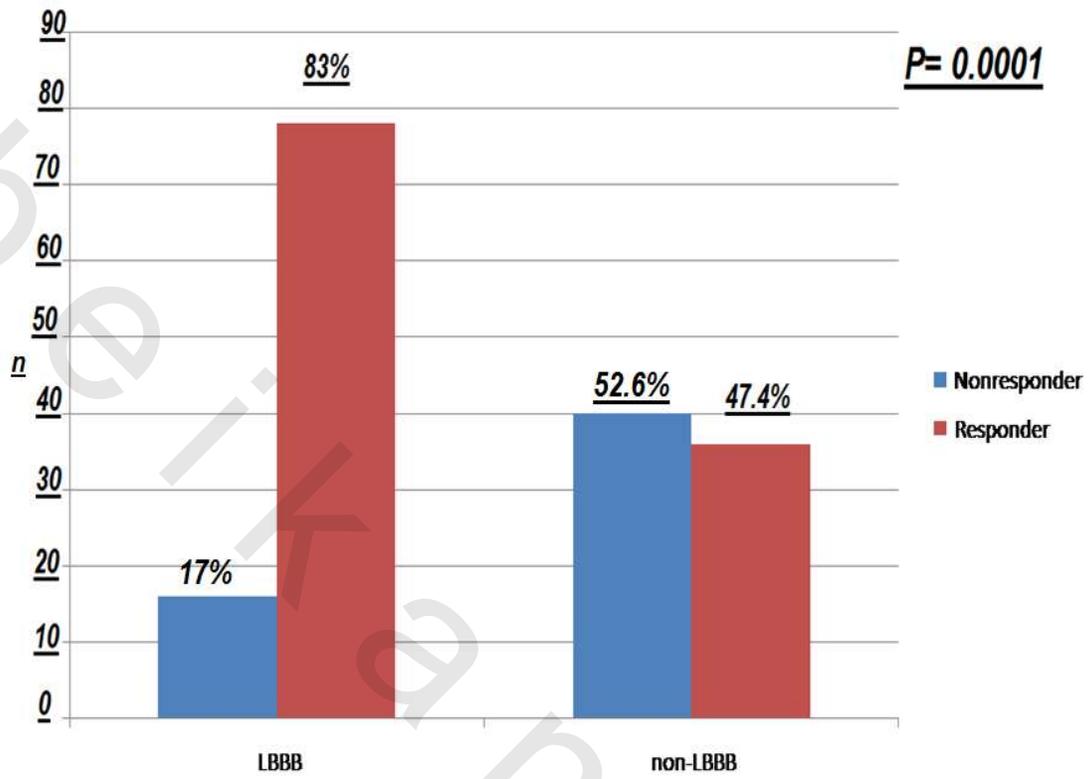


Figure 3.6: QRS morphology and response

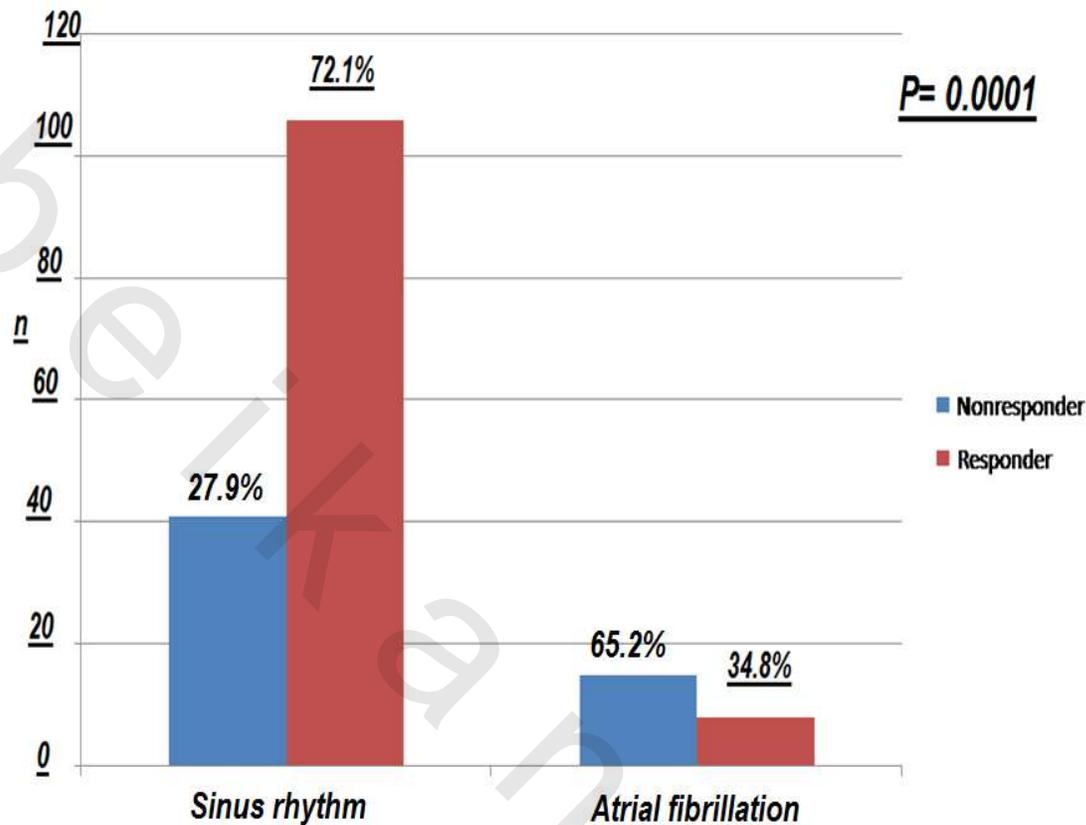


Figure 3.7: Rhythm at CRT implantation and CRT response

Echocardiography:

The presence of RV dysfunction defined as TAPSE <15 mm was an independent predictor of nonresponse in multinomial logistic regression (OR 3.4; 95% CI 1.1-10.4, P=0.036). Patients with baseline TAPSE \geq 15 mm had better response rate than those with baseline TAPSE < 15 mm (76.1% vs. 50.8% respectively, P=0.001).

Baseline RV dilatation was associated with CRT nonresponse; 57.1% of patients with dilated RV (RVd>35mm) were responders vs. 75.3% of those with RVd \leq 35mm, P=0.012. Presence of more than mild pulmonary hypertension was associated with reduced response rate to CRT. The response rate was 78%, 71% and 51% for no PHT, mild PHT, more than mild PHT respectively, P= 0.027. Both RV dilatation and PHT were not significant predictors of CRT response in multinomial logistic regression analysis.

Fifty-one patients had grade I diastolic dysfunction, 74% of them responded to CRT. Fifty-three patients had grade II diastolic dysfunction, 70% of them responded to CRT. Forty-three patients had grade III diastolic dysfunction, 51% of them responded to CRT. Patients with grade III diastolic dysfunction were less likely to respond to CRT compared to patients with less than grade III diastolic dysfunction (51.5% vs. 70.8% respectively, P=0.034). The probability of CRT response was not related to the severity of baseline mitral regurgitation or the left ventricular dimensions, volumes nor function.

As regards the echocardiographic markers of dys-synchrony, septal-posterior wall motion delay (SPWMD), interventricular delay (IVD) and the delay between time to peak systolic velocity in ejection phase at basal septal and basal lateral segments (Ts-septal-lateral) were significant predictors of CRT response in univariate analysis. The CRT response was 77% in patients with SPWMD \geq 130 msec vs. 58% of those with SPWMD<130 msec, P= 0.02. The CRT response rate was 74% when Ts-septal-lateral \geq 60 msec vs. 63% when Ts-septal-lateral <60 msec, P= 0.043. Also, 74% of patients with IVD \geq 40 msec were responders vs. 63% of patients with IVD <40 msec, P= 0.04. However, in multinomial logistic regression analysis, none of them proved to be an independent predictor of CRT response.

| Baseline echocardiography | | Nonresponders n=56 | Responders n= 114 | P |
|---------------------------|---|-----------------------|----------------------|-------|
| RV function | TAPSE <15 mm | 30 (49.2%) | 31 (50.8%) | 0.001 |
| | TAPSE \geq 15 mm | 26 (23.9%) | 83 (76.1%) | |
| Right side dilatation | RVd<35 mm | 23 (24.7%) | 70 (75.3%) | 0.012 |
| | RVd \geq 35 mm | 33 (42.9%) | 44 (57.1%) | |
| PHT | PAP \leq 50 mmhg | 39 (28.9%) | 96 (71.1%) | 0.027 |
| | PAP>50 mmhg | 17 (48.6%) | 18 (51.4%) | |
| Diastolic dysfunction | Less than grade III diastolic dysfunction | 30 (29.2%) | 73 (70.8%) | 0.034 |
| | Grade III diastolic dysfunction | 21 (48.8%) | 22 (51.2%) | |

| | | | | |
|-------------------------|-----------------|------------|------------|------|
| Mitral regurgitation | No/mild | 40 (35%) | 74 (65%) | 0.8 |
| | Moderate/severe | 16 (29%) | 40 (71%) | |
| Tricuspid regurgitation | No/mild | 41 (30%) | 92 (70%) | 0.4 |
| | Moderate/severe | 15 (39%) | 22 (61%) | |
| LVIDd | <65 mm | 30 (35.5%) | 53 (64.5%) | 0.8 |
| | ≥ 65mm | 26 (32.1%) | 61 (67.9%) | |
| LVIDs | <55mm | 26 (35%) | 51 (65%) | 0.9 |
| | ≥55mm | 30 (34%) | 63 (66%) | |
| LVFT/RR% | <40% | 21 (30%) | 50 (70%) | 0.4 |
| | ≥40% | 35 (35%) | 64 (65%) | |
| IVD | <40msec | 30 (37%) | 49 (63%) | 0.04 |
| | ≥40msec | 26 (26%) | 65 (74%) | |
| LVPEI | <140msec | 36 (37%) | 66 (63%) | 0.5 |
| | ≥140msec | 20 (31%) | 48 (69%) | |
| SPWMD | <130msec | 35 (42%) | 49 (58%) | 0.02 |
| | ≥130msec | 21 (23%) | 65 (77%) | |
| Ts-septal-lateral | <60msec | 32 (37%) | 54 (63%) | 0.04 |
| | ≥60msec | 24 (26%) | 60 (74%) | |

Table 3.12: Echocardiography and CRT response

Etiology and CRT response:

Non-ischemic cardiomyopathy was an independent predictor of response (OR 3.1; 95% CI 1.1-8.4, P= 0.028). The CRT response rate among patients with N-ICM was 80.2% vs. 51.9% in patients with ischemic cardiomyopathy, P<0.0001. Patients with ICM without previous infarction were not significantly different from those who experienced previous myocardial infarction. Previous revascularization did not induce significant difference in response rate among ischemic patients.

| Etiology | Nonresponders | Responders | P |
|----------|---------------|------------|---|
|----------|---------------|------------|---|

| | n=56 | n=114 | |
|-------------------------------|------------|------------|--------|
| ICM | 38 (48.1%) | 41 (51.9%) | 0.0001 |
| N-ICM | 18 (19.8%) | 73 (80.2%) | |
| Previous infarction | 23 (53.5%) | 20 (46.5%) | 0.2 |
| No previous infarction | 15 (41.7%) | 21 (58.3%) | |
| Previous revascularization | 29 (48.3%) | 31 (51.7%) | 0.9 |
| No previous revascularization | 9 (47.4%) | 10 (52.6%) | |

Table 3.13: Etiology and revascularization vs. CRT response

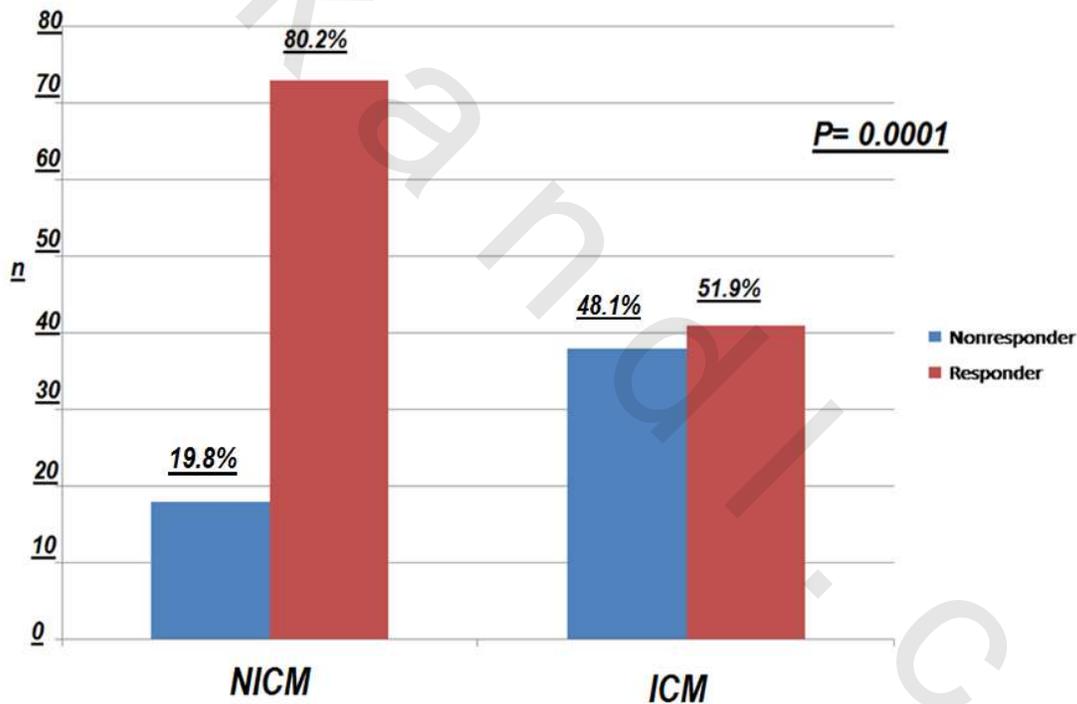


Figure 3.8: Etiology and CRT response

Device optimization and CRT response:

Device optimization using device based automated algorithms was performed at the same implantation day in 57.6% of patients. The AV delay was set empirically at 120 msec and VV delay at 0 msec in patients with no device optimization. Device optimization was done in the nonresponders at 6 months with no improvement in NYHA class at 12 months post-implantation.

There was no significant difference in CRT response rate between patients underwent device optimization and others who didn't undergo device optimization (69.4% vs. 63.9% respectively, P= 0.09).

LV lead position and response:

Optimal short axis and long axis position of the LV lead was associated with improved response to CRT. Patients with LV leads in a lateral, posterior or posterolateral position compared to anterior and anterolateral positions were more likely to be responders (74.9% vs. 53.3%, P=0.005), also they had better LVEF after 6 months (37.4+10.5 vs. 28.9+11.9, P=0.002).

Patients with LV leads in the apical position compared to basal and mid cavity positions had significantly higher heart failure related mortality rates at 1 year (44.4% vs. 6.8%, P<0.001, P=0.0001) and lower LVEF after 6 months (27.1+7.8 vs. 36.8+11, P=0.007). Optimal LV lead position (combined optimal long axis and short axis position) was an independent predictor of CRT response (OR 11.3; 95% CI 2-63.8). The CRT response rate with optimal LV lead position was 71.2% vs. 29.4% with non-optimal LV lead position, P<0.0001.

| LV lead position | | Nonresponders n=56 | Responders n=114 | P |
|------------------|------------------|-----------------------|---------------------|--------|
| Short axis | Non-optimal | 7 (70.0%) | 3 (30.0%) | 0.01 |
| | Optimal position | 49 (30.6%) | 111 (69.4%) | |
| long axis | Non-optimal | 7 (77.8%) | 2 (22.2%) | 0.003 |
| | Optimal position | 49 (30.4%) | 112 (69.6%) | |
| LV lead position | Non-optimal | 12 (70.6%) | 5 (29.4%) | 0.0001 |
| | Optimal | 44 (28.8%) | 109 (71.2%) | |

Table 3.14: LV lead position and CRT response

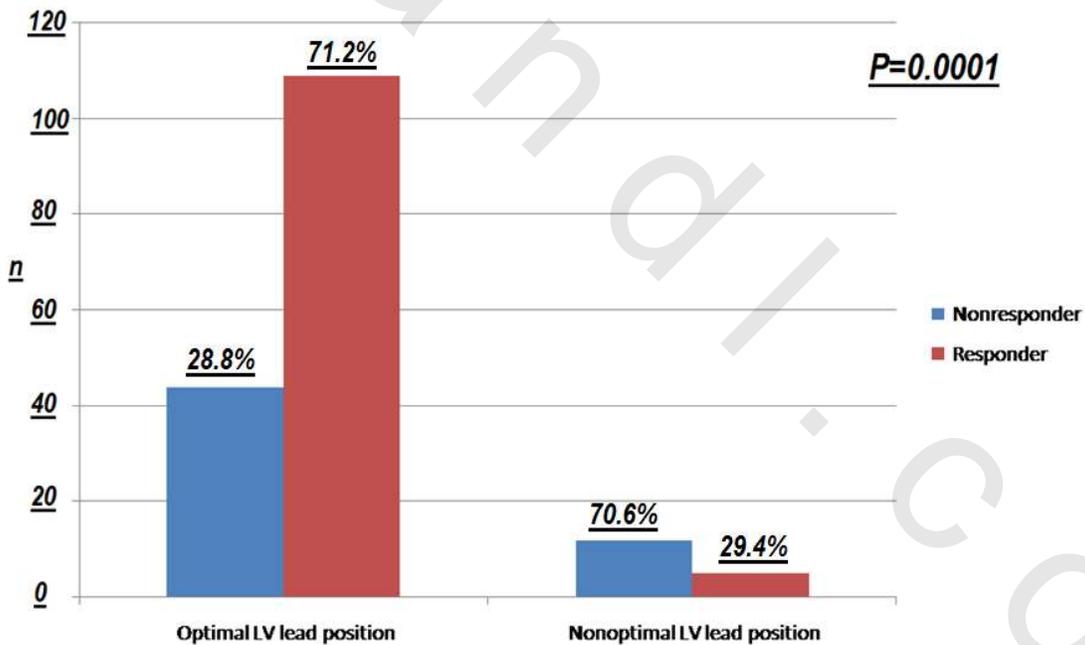
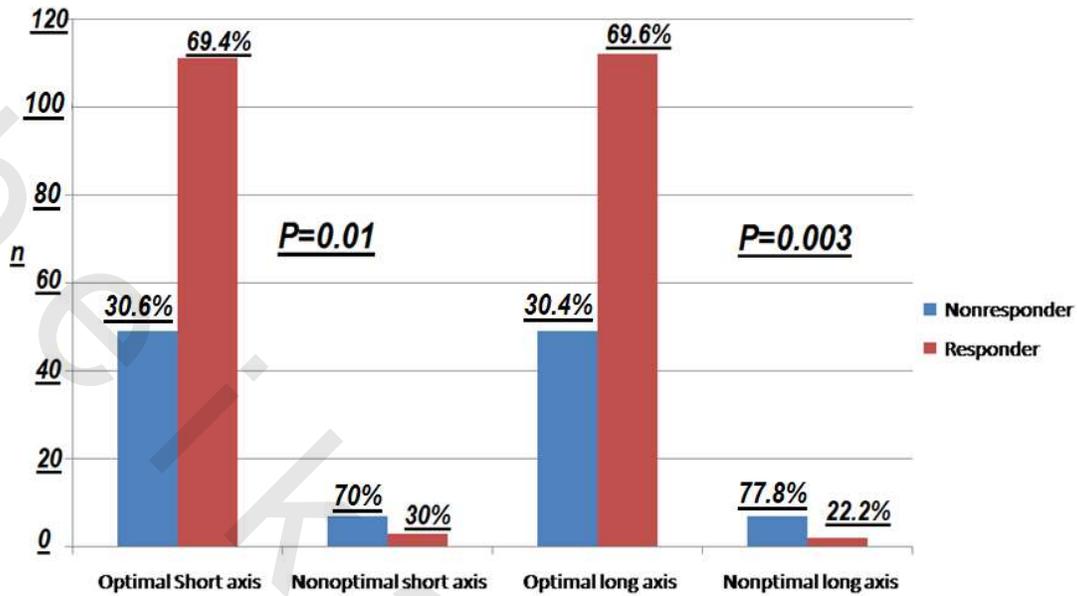


Figure 3.9: LV lead position and CRT response

New score to predict CRT response:

We developed a new simple CRTscore based on preimplantation date to predict CRT response. The CRTscore consists of maximum 9 point. Initially all significant independent preimplantation predictors of CRT response in

multinomial logistic regression analysis were included in the CRTscore according to their relative effect in the regression model to generate an initial CRTscore. It has been shown that the magnitude of benefit from CRT is highest in patients with wider QRS complex, LBBB, female gender and nonischemic cardiomyopathy (figure 3.10).⁽⁴⁶⁾

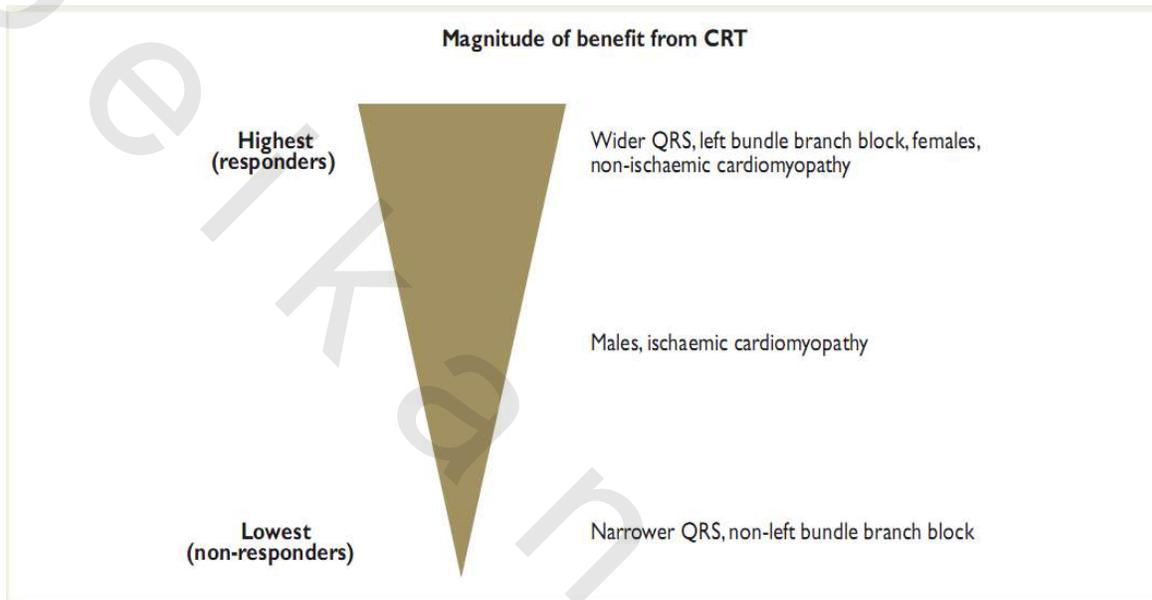


Figure 3.10: Magnitude of benefit from CRT⁽⁴⁶⁾

When LBBB and female gender were added to other variables, the statistical power of the score increased, so they were included in the final CRTscore. The CRTscore includes QRS duration ≥ 150 msec, LBBB morphology of the QRS complex, non-ischemic etiology of cardiomyopathy, sinus rhythm at time of CRT implantation, preserved RV function with TAPSE ≥ 15 mm, female gender, absence of history of renal disease and finally absence of significant COPD (based on specialized respiratory assessment and use of specific medications). Each parameter was assigned to a single point except QRS duration ≥ 150 msec was assigned to 2 points. The CRTscore is the sum of all points.

| Parameter | Points |
|--------------------|--------|
| QRS \geq 150msec | 2 |
| LBBB | 1 |
| NICM | 1 |
| Sinus rhythm | 1 |
| Female gender | 1 |

| | |
|------------------------------------|---|
| TAPSE\geq15mm | 1 |
| No history of renal disease | 1 |
| No lung disease | 1 |
| Total | 9 |

Table 3.15: Points in the CRTscore

The CRT response rate has been markedly different according to the CRTscore. Patients with CRTscore ≥ 6 had CRT response rate of 97.5% vs. only 40.7% if CRTscore <6 , $P<0.001$.

| CRTscore | Nonresponders (n) | Responders (n) | Response rate |
|----------|-------------------|----------------|---------------|
| 0 | 1 | 0 | 0% |
| 1 | 3 | 0 | 0% |
| 2 | 9 | 2 | 18.2% |
| 3 | 18 | 6 | 25% |
| 4 | 11 | 12 | 52.2% |
| 5 | 12 | 17 | 58.6% |
| 6 | 2 | 28 | 93.3% |
| 7 | 0 | 18 | 100% |
| 8 | 0 | 22 | 100% |
| 9 | 0 | 9 | 100% |
| Total | 56 | 114 | 67.1% |

Table 3.16: CRT response according to the CRTscore

| CRTscore | Nonresponders n= 56 | Responders n= 114 | P |
|----------|------------------------|----------------------|--------|
| <6 | 54 (59.3%) | 37 (40.7%) | 0.0001 |
| ≥ 6 | 2 (2.5%) | 77 (97.5%) | |

Table 3.17: CRT response in patients with CRTscore ≥ 6

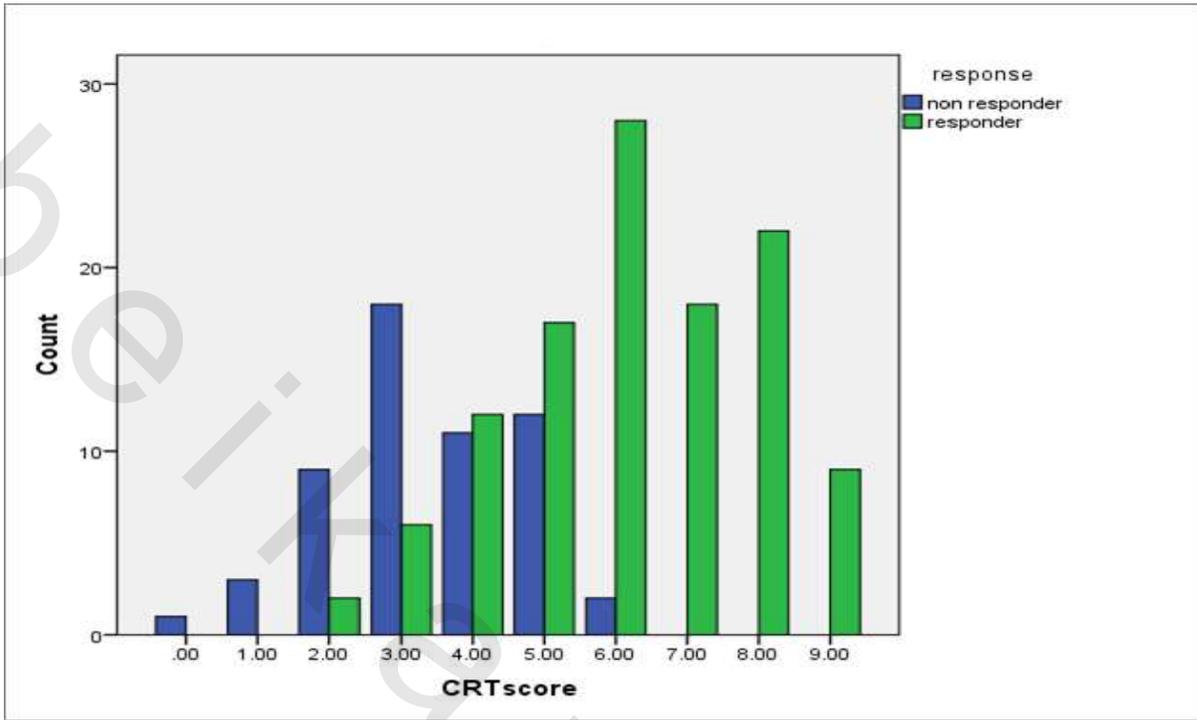


Figure 3.11: CRT response according to the CRTscore

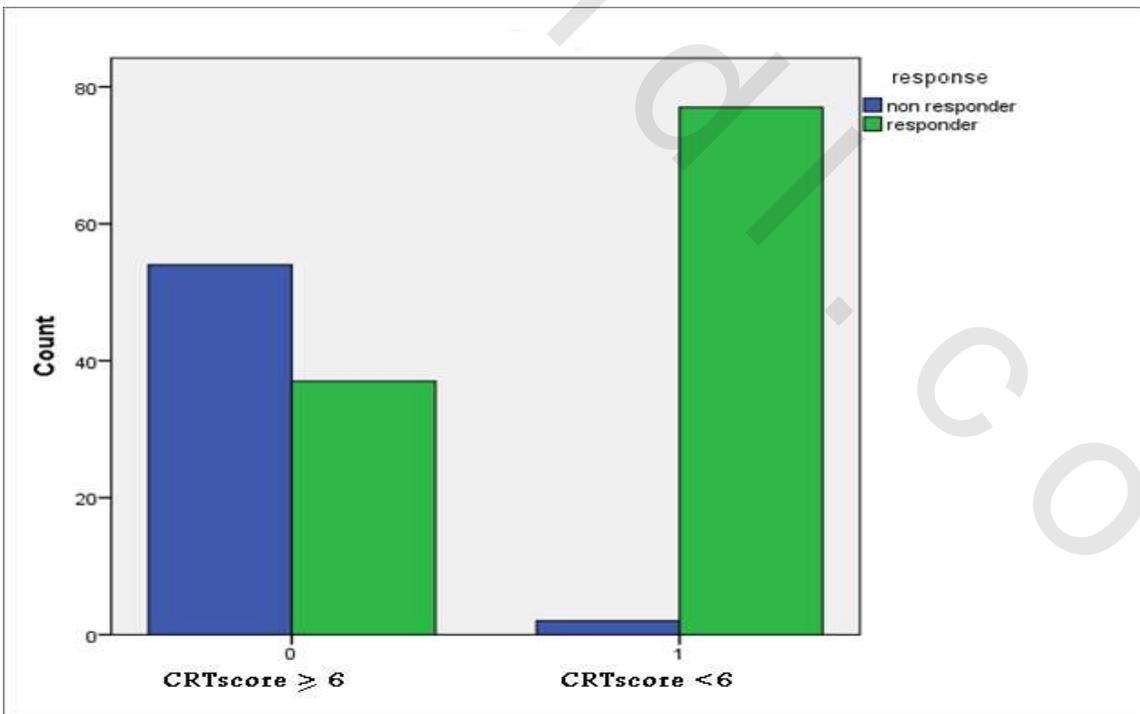


Figure 3.12: CRT response in patients with CRTscore ≥ 6

The CRTscore in the scope of guidelines

According to the 2013 European Society of Cardiology guidelines on cardiac pacing and CRT, 87 of our patients met class I indication for CRT implantation, 33 met class IIa indication , 25 patients met class IIb and 25 met class III indication for CRT implantation.⁽⁴⁶⁾

Patients with class I indication for CRT implantation had a response rate of 85%. The CRTscore was ≥ 6 in 68 patients (66 (97%) responders and 2 (3%) nonresponders), while the CRTscore was less than 6 in 19 patients (8 (42.1%) responders and 11 (57.9%) nonresponders, P <0.0001).

| CRTscore | Nonresponders (n) | Responders (n) | Response rate |
|----------|-------------------|----------------|---------------|
| 2.00 | 1 | 0 | 0% |
| 3.00 | 1 | 0 | 0% |
| 4.00 | 3 | 2 | 40% |
| 5.00 | 6 | 6 | 50% |
| 6.00 | 2 | 20 | 90.9% |
| 7.00 | 0 | 15 | 100% |
| 8.00 | 0 | 22 | 100% |
| 9.00 | 0 | 9 | 100% |
| Total | 13 | 74 | 85.1% |

Table 3.18 : CRTscore and response in patients with class I indication

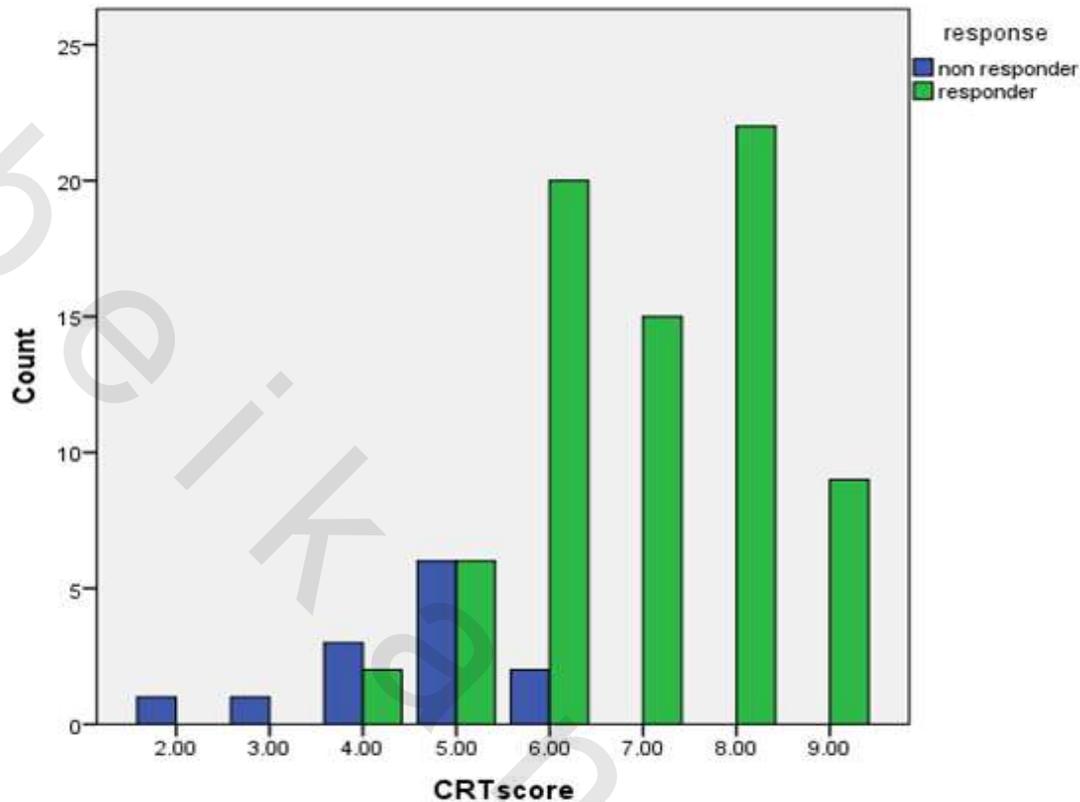


Figure 3.13 : CRTscore and response in patients with class I Indication

Patients with class IIa indication for CRT implantation had a response rate of 48.5%. The CRTscore was ≥ 6 in 9 patients (9 (100%) responders), while the CRTscore was less than 6 in 24 patients (7 (29.2%) responders and 17 (70.8%) nonresponders, $P < 0.0001$).

| CRTscore | Nonresponders (n) | Responders (n) | Response rate |
|----------|-------------------|----------------|---------------|
| 0 | 1 | 0 | 0% |
| 1 | 1 | 0 | 0% |
| 2 | 2 | 0 | 0% |
| 3 | 4 | 1 | 20% |
| 4 | 4 | 2 | 33.3% |
| 5 | 5 | 4 | 44.4% |
| 6 | 0 | 6 | 100% |
| 7 | 0 | 3 | 100% |

| | | | |
|-------|----|----|-------|
| Total | 17 | 16 | 48.5% |
|-------|----|----|-------|

Table 3.19 : CRTscore and response in patients with class IIa indication

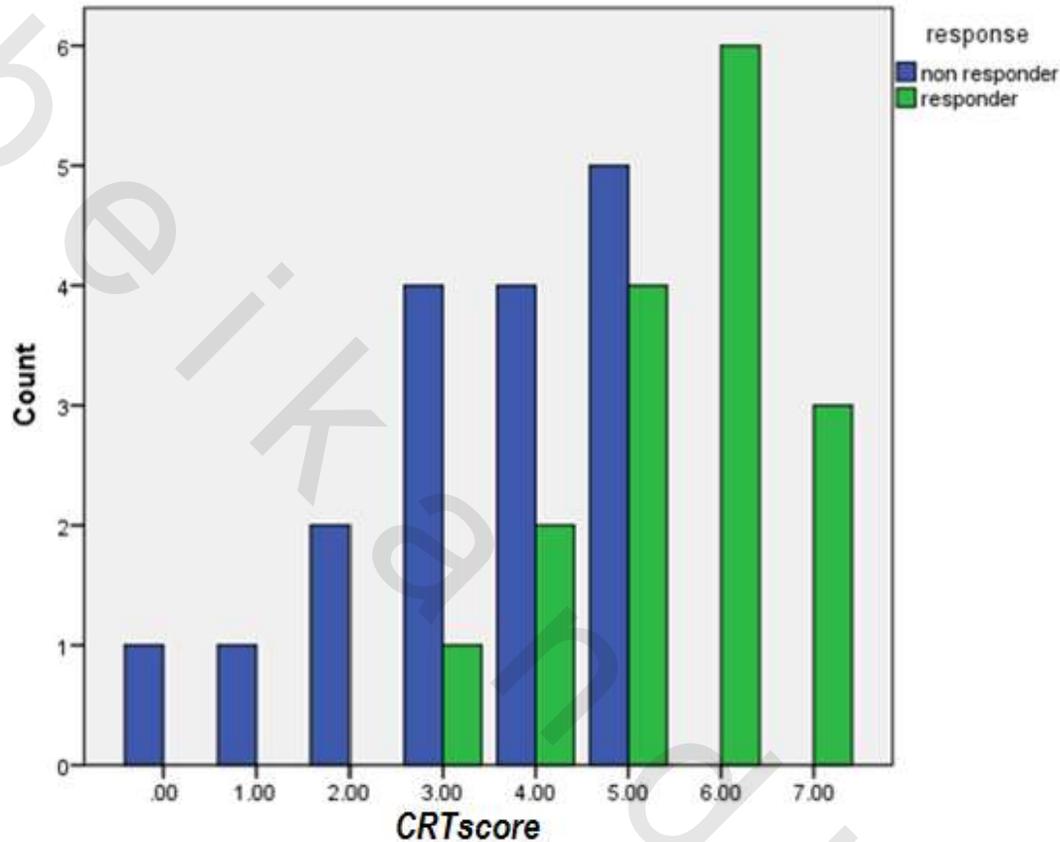


Figure 3.14 : CRTscore and response in patients with class IIa indication

Patients who met class IIb or III indication for CRT implantation had a response rate of 48%. The CRTscore was ≥ 6 in 2 patients (both are responders), while the CRTscore was less than 6 in 48 patients (22 responders and 26 nonresponders). Most of the nonresponders had a CRTscore < 4 . The CRT response was better in patients with CRTscore ≥ 4 compared to those with lower CRTscore (77.3% vs 25%, $P < 0.001$).

| CRTscore | Nonresponders (n) | Responders (n) | Response rate |
|----------|-------------------|----------------|---------------|
| 1 | 2 | 0 | 0% |
| 2 | 6 | 2 | 25% |
| 3 | 13 | 5 | 27.8% |
| 4 | 4 | 8 | 66.7% |
| 5 | 1 | 7 | 87.5% |

| | | | |
|-------|----|----|------|
| 6 | 0 | 2 | 100% |
| Total | 26 | 24 | 48% |

Table 3.20 : CRTscore and response in patients with class IIb/III indication

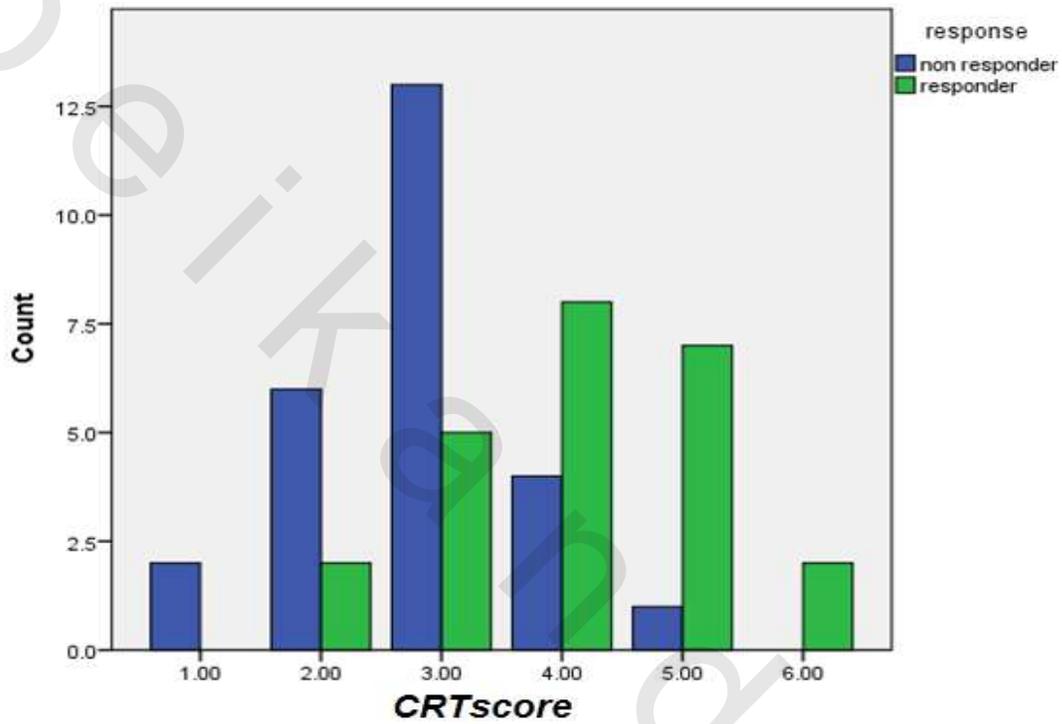


Table 3.15 : CRTscore and response in patients with class IIb/III indication

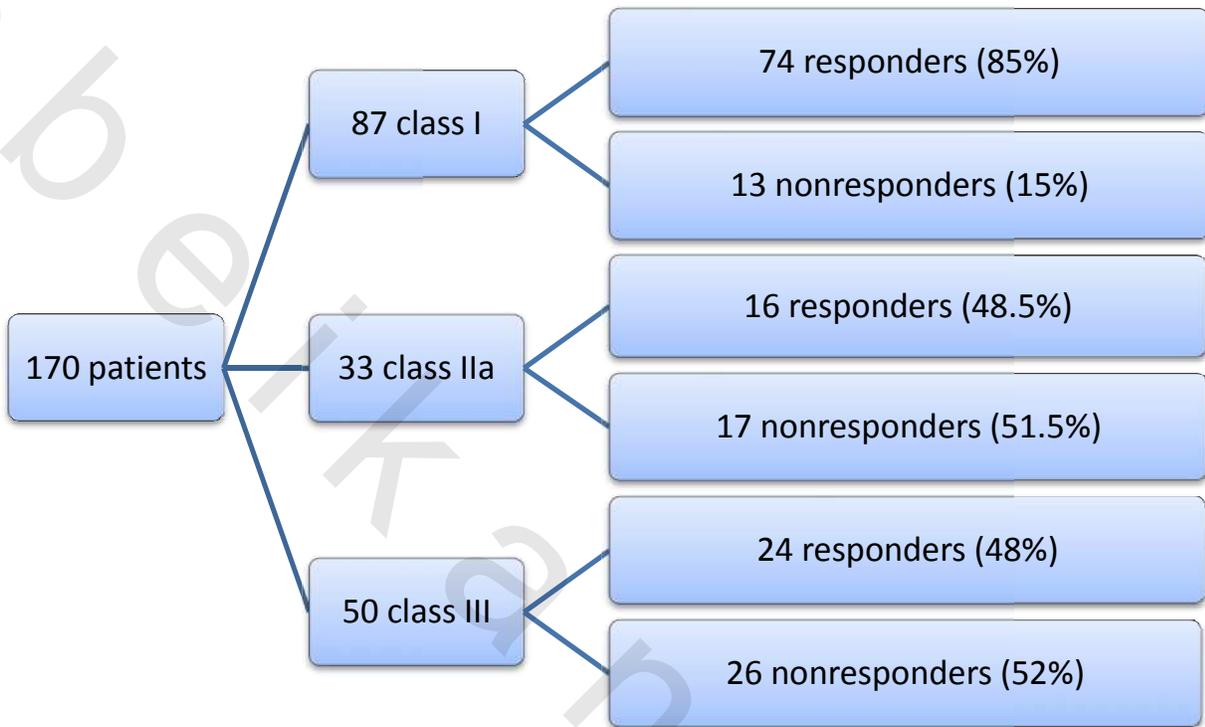


Figure 3.16: Guidelines and CRT response

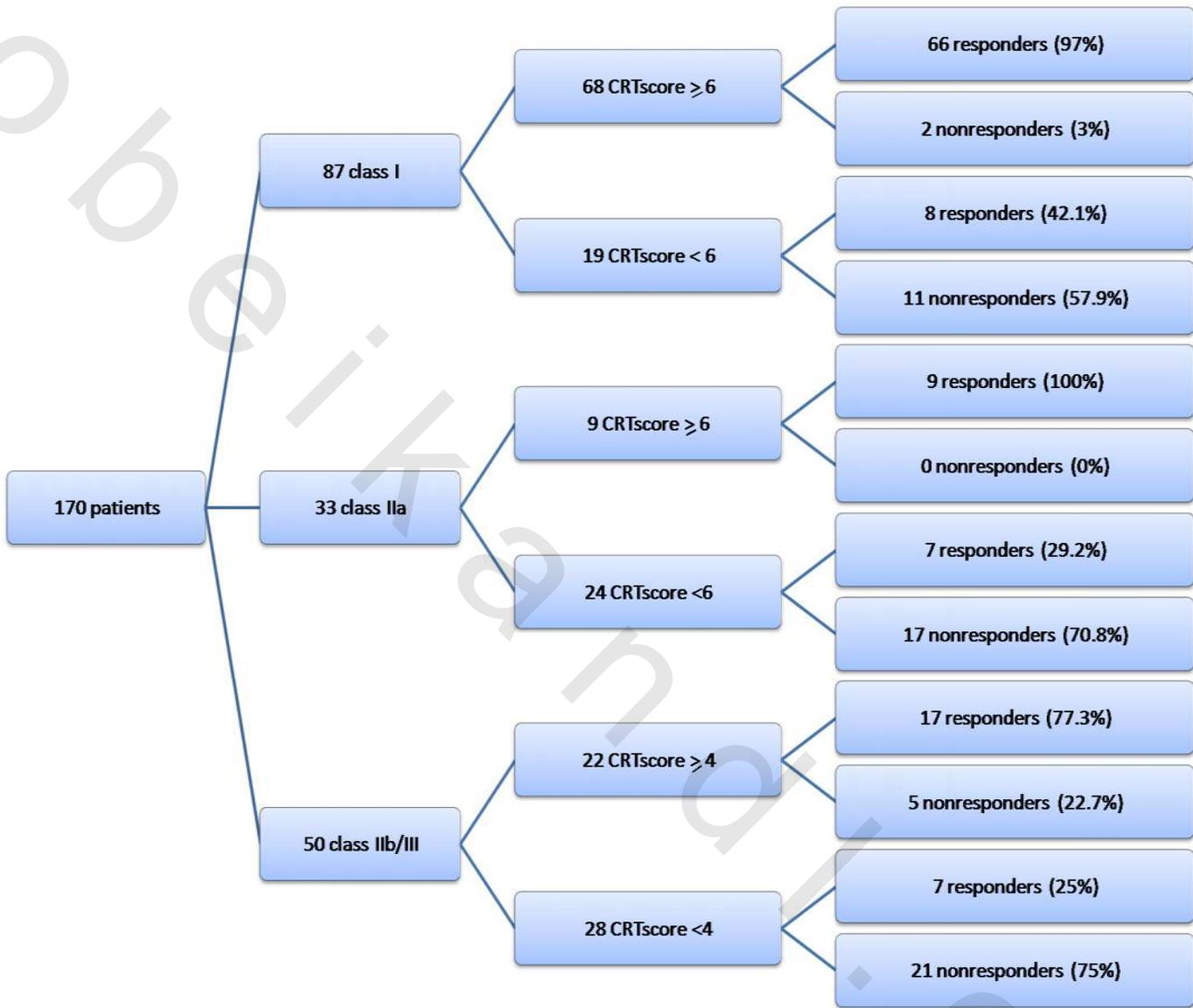


Figure 3.17: Guidelines, CRTscore and CRT response