On-Pump/Beating-Heart Myocardial Protection for Isolated or Combined Coronary Artery Bypass Grafting in Patients with Severe Left Ventricle Dysfunction: Assessment of Myocardial Function and Clinical Outcome

Oner Gulcan, MD,1 Rıza Turkoz, MD,1 Ayda Turkoz, MD,2 Esra Caliskan, MD,2 Alpay T. Sezgin, MD3
Departments of 1Cardiovascular Surgery, 2Anesthesiology, and 3Cardiology, Adana Teaching and Medical Research Center, Baskent University, Adana, Turkey

ABSTRACT

Background: Myocardial protection in coronary artery bypass grafting (CABG) with severe left ventricular (LV) dysfunction is still a surgical dilemma. Preoperative myocardial infarction (MI) and postoperative low output syndrome are serious complications in cases of inadequate protection of the heart, which has limited myocardial reserve. The aim of this study was to evaluate myocardial function and clinical outcome after on-pump/beating-heart CABG in patients with severe LV dysfunction.

Methods: Between March 2001 and March 2004, clinical, operative, and postoperative data were prospectively collected from patients with LV ejection fraction (EF) ≤30% who underwent on-pump/beating-heart CABG and associated procedures.

Results: There were 46 patients and the mean patient age was 58.38 ± 9.23. The mean EF was 25.6 ± 2.8%. Operating time was 275 ± 63 minutes. The frequency of distal anastomosis was 3.06 ± 1.04. Twenty-four patients required aneurysmectomy in addition to CABG, and 2 of the 24 required mitral repairs. Inotropic support was required in 14 patients (30%) and 5 of them (10.9%) also required IABP. The LV EF improved significantly after the operation when compared to preoperative measurements (25.6 ± 2.8 versus 33.6 ± 4.69, \(P < .05\)). Hospital mortality rate was 4.3% (2 of the 46 patients). No mortality was observed at a mean follow-up of 16 months after discharge from the hospital.

Conclusions: On-pump/beating-heart CABG technique is effective in protecting myocardial functions in patients with severe LV dysfunction. The main advantage of the on-pump/beating-heart technique is the ability it provides one to perform complete revascularization, and intracavitary procedures with low morbidity and mortality even in impaired LV function.

INTRODUCTION

Research has shown that coronary artery bypass grafting (CABG) has a greater positive impact on survival and quality of life than medical therapy in cases of severe left ventricular (LV) dysfunction [Elefteriades 1995, Mickleborough 1995, Pigott 1985, Scott 1994]. Improvement in myocardial protection techniques and complete revascularization procedures has reduced the rates of morbidity and mortality associated with CABG. However, perioperative morbidity and mortality remain high in patients with severe LV dysfunction who undergo this procedure [Kaul 1996]. Recently, beating-heart and non-cardioplegic CABG have been used as alternative surgical techniques in high-risk patients [Alfieri 1999, Antunes 1999, Ascione 1999, 2003, Goldstein 2003, Meharwal 2002]. The beating-heart technique has surgical limitations with respect to achieving complete revascularization, especially if the patient has LV dysfunction and severe cardiomegaly; also, intracavitary approach is impossible with this technique. The aim of this study was to evaluate the myocardial function and clinical outcome after on-pump/beating-heart CABG and combined procedures (aneurysmectomy and mitral repair) in patients with severe LV dysfunction.

MATERIAL AND METHODS

From March 2001 to March 2004, data were prospectively collected from patients with ejection fraction (EF) ≤30% who underwent on-pump/beating-heart CABG and associated procedures, specifically aneurysmectomy and mitral valve repair. EF was determined preoperatively from ventriculography and transthoracic echocardiography in each case. Postoperative EF measurements were obtained by transthoracic echocardiography during the third month follow-up. The decision whether a patient would undergo the procedure on-pump was made by the surgeons (RT, OG).

Carotid artery Doppler ultrasound was performed if a patient was older than 60 years of age or had carotid bruit, diabetes mellitus, peripheral vascular disease, or left main coronary artery disease. Atherosclerosis of the ascending aorta was evaluated preoperatively with computerized tomography (CT) in patients over 70 years of age, and in individuals with carotid bruit, diabetes mellitus, peripheral vascular disease, or left main
Table 1. The Preoperative Data for the Study Group

<table>
<thead>
<tr>
<th>Variable, n (%)</th>
<th>On-pump/beating (n = 46)</th>
</tr>
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<tbody>
<tr>
<td>Age (yrs)*</td>
<td>57.9 ± 9.5</td>
</tr>
<tr>
<td>Male/Female</td>
<td>39/7</td>
</tr>
<tr>
<td>Diabetes</td>
<td>12 (26.1)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>19 (41.3)</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>16 (34.8)</td>
</tr>
<tr>
<td>CHF</td>
<td>13 (28.2)</td>
</tr>
<tr>
<td>MI</td>
<td></td>
</tr>
<tr>
<td>Old</td>
<td>28 (60.8)</td>
</tr>
<tr>
<td>Recent (&lt;30 days)</td>
<td>7 (15.2)</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>2 (4.3%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>11 (23.9%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>32 (69.6%)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>4 (8.7%)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>9 (19.6%)</td>
</tr>
<tr>
<td>Atherosclerotic aorta</td>
<td>9 (19.6%)</td>
</tr>
<tr>
<td>Renal failure (creatinine &gt; 2 mg/dL)</td>
<td>1 (2.2%)</td>
</tr>
<tr>
<td>COPD</td>
<td>8 (17.4%)</td>
</tr>
<tr>
<td>NYHA Class*</td>
<td>3.06 ± 0.77</td>
</tr>
<tr>
<td>Unstable</td>
<td>21 (45.7)</td>
</tr>
<tr>
<td>Redo case</td>
<td>2 (4.3%)</td>
</tr>
<tr>
<td>Preoperative IABP</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Ejection fraction (%)*</td>
<td>25.6 ± 2.8</td>
</tr>
<tr>
<td>Euro score*</td>
<td>7.1 ± 3.7</td>
</tr>
</tbody>
</table>

*Values are shown as mean ± standard deviation.

CAD indicates coronary artery disease; CHF, congestive heart failure; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association; IABP, intraaortic balloon pump.

coronary artery disease. Nineteen patients had undergone preoperative myocardial scintigraphic evaluation. However, viability tests including myocardial perfusion scintigraphy, positron emission tomography, and stress echocardiography were not considered decisive in establishing indications for surgery, CAGB was scheduled only if coronary angiography showed distal target vessels suitable for bypass graft placement.

Anesthesia
Each patient received his or her routine cardiac medication prior to surgery and was premedicated with midazolam 10 mg per os 1 hour before the operation. Anesthesia was induced with intravenous injections of fentanyl (25 µg/kg) and thiopental (3 mg/kg), and intubation was facilitated with vecuronium (0.08 mg/kg). Anesthesia was maintained with a continuous infusion of fentanyl (8 µg/kg/h) and midazolam (0.2 µg/kg/min). Muscle relaxation was achieved with intravenous injections of vecuronium (0.02 mg/kg/every 30 min). A pulmonary artery catheter (TD thermodilution, Abbot Laboratories, Chicago, IL, USA) was placed via the right internal jugular vein after induction of anesthesia. After cardiopulmonary bypass (CPB), dobutamine and dopamine were administered as needed.

Surgery
A median sternotomy was performed in each case. The left internal mammary artery, radial artery, and saphenous vein were harvested using standard techniques. CPB was initiated using the ascending aorta or femoral artery and two-stage venous cannulation. The site to be used for arterial cannulation was determined according to the severity of the atherosclerotic disease in the ascending aorta, as assessed by CT. A membrane oxygenator (Cobe Optima XP, CO, USA) was used in all operations. Tepid hypothermia (33°C) was maintained during CPB. When a patient required aneurysmectomy, a left atrial vent was placed through the right superior pulmonary vein. LV aneurysm repair and CAGB were performed consequently on each beating heart without aortic cross-clamping. Left ventriculotomy was performed 2 cm lateral to the left anterior descending artery while the pump was on. The border zone between normal and nonviable myocardium was observed in the ventricle. A 2-0 prolene suture was placed around the border zone (Fontan stitch) and tied down at the proper tension. If the diameter of the new opening in the left ventricle was less than 2 cm, the opening was closed by a modified linear closure technique. If the hole was larger, it was closed with a synthetic patch. Associated mitral valve regurgitation was managed with double-orifice repair. For this, central edge-to-edge suturing was performed via access through the cavity of the left ventricle before LV aneurysm repair [Alfieri 1999]. Mitral repair was performed in patients who had severe (grade 3 or 4) mitral insufficiency.

A tissue stabilizer (Octopus 2, Medtronic Inc, Minneapolis, MN, USA) or an epicardial retracting stabilizer (Chase medical, Richardson, TX, USA) was used to stabilize the target coronary vessel. The target vessel was occluded proximally using a double loop with a vascular loop (surg-I-loop plus, Scanlan, St. Paul, MN, USA) or an 8-mm bulldog clamp. The distal portion of the vessel was occluded when excessive backflow began to obstruct the surgeon's view. A carbon dioxide blower was used routinely. For proximal anastomosis, the target vessel was attached to the ascending aorta, or to the left internal mammary artery in cases of aortic arteriosclerosis.

Perioperative myocardial infarction (MI) was diagnosed on the basis of postoperative electrocardiography findings: development of new Q waves, loss of R wave progression, or a new ST interval and T-wave changes in association with a >5% increase in serum creatine kinase-myocardial band isoenzyme (CK-MB): CK ratio. Inotropic support was defined as a requirement of inotrope administration for more than 30 minutes. A patient was considered to be in respiratory failure if they required mechanical ventilation for more than 48 hours. Hospital mortality was defined as death in the first 30 days after the operation.

The preoperative risk factors, intraoperative variables, and postoperative results were recorded.

RESULTS

The same surgical team performed CAGB on a total of 1138 patients during the study period. Eighty-one of these patients had EF ≤30%, and 46 of these individuals who underwent on-pump/beating-heart CAGB participated in the study. The other 12 patients underwent conventional CAGB with aortic cross-clamping, and 37 who underwent off-pump/beating heart were, therefore, excluded.

The patients' preoperative characteristics are summarized in Table 1. Patients were young (58.38 ± 9.23 years). The
mean LV EF value was 25.6 ± 2.8%. The coronary angiography findings revealed that 67.9% of the patients had triple-vessel disease and 23.9% had double-vessel disease.

The operative data are summarized in Table 2. The study group had a 3.06 ± 1.04 total number of distal anastomoses. In the four patients who had atherosclerotic disease in the ascending aorta atherosclerosis. In the group had a 3.06 ± 1.04 total number of distal anastomoses.

The number of anastomoses* 3.06 ± 1.04

Distal anastomoses
- Left anterior descending artery 43 (93.5)
- Diagonal branch 28 (60.8)
- Right coronary artery 34 (73.9)
- Obtuse marginal branch 35 (76.1)
- Endarterectomy (LAD) 2 (4.3)
- Endarterectomy (carotid artery) —
- Aneurysmectomy 24 (52.2)
- Mitral repair 2 (4.3)
- Postinfarction VSD repair 1 (2.2)
- No-touch aorta technique 5 (10.9)
- CPB time (min)* 94.71 ± 34.41 (min 25, max 160)
- Operating time (min) 275 ± 69
- Perioperative myocardial infarction 1 (2.2)

*Values are shown as mean ± standard deviation.

LIMA indicates left internal mammary artery; RIMA, right internal mammary artery; GEA, gastroepiploic artery; LAD, left anterior descending artery; VSD, ventricular septal defect; CPB, cardiopulmonary bypass.

This study documented the results of on-pump/beating-heart method CABG and associated procedures in patients with severe LV dysfunction. Most similar investigations of patients with impaired LV function have compared off-pump/beating-heart and conventional CABG [Ascione 2003, Goldstein 2003, Meharwal 2002]. The majority of results have revealed lower morbidity and mortality with the off-pump/beating heart method than with conventional CABG [Ascione 2003, Goldstein 2003, Meharwal 2002]. In our study, we found low morbidity and mortality rates, even though our patients had a high frequency of complications such as LV aneurysms and mitral insufficiency.

Research has revealed higher mortality and morbidity with CABG in patients with severe LV dysfunction (EF < 30%) compared to CABG in patients with normal LV function [Christakis 1992]. Individuals with EF <30% have little or no ventricular function reserve and, therefore, do not tolerate perioperative myocardial injury well. Most cardiac surgeons use CPB with aortic cross-clamping and various blood cardioplegic modifications when performing CABG. Despite blood cardioplegic protection, lactate release with low cardiac output has been shown after release of the aortic cross-clamping in coronary bypass surgery [Rao 2001]. Return to normal aerobic lactate extraction and functional recovery may be delayed for as long as 4 hours after cross-clamp removal [Rao 2001].
Recently, off-pump coronary revascularization has become more popular, particularly for high-risk cases, which include patients with poor LV function [Meharwal 2002, Moshkovits, 1997, Sternik 1997]. Reports published to date have shown lower morbidity and mortality in off-pump patients than in on-pump patients; however, the off-pump groups had lower frequencies of distal anastomosis and circumflex artery system anastomosis [Meharwal 2002, Moshkovits, 1997, Sternik 1997]. One negative aspect of the off-pump technique is lower patency rates [Khan 2004, Omeroglu 2000]. Experienced surgical teams using new stabilization devices, and exposure systems are now successfully performing revascularization in the region of the circumflex system. Even when new stabilization devices and exposure systems are used with the off-pump technique, in patients with severely impaired LV function and advanced cardiomegaly (end-diastolic volume >200 mL), it may not be possible to access the lateral region of the heart properly for revascularization. Reports on two large series operated with the off-pump technique have documented successful multivessel coronary revascularization in patients with LV dysfunction [Goldstein 2003, Meharwal 2002]. However, it is still difficult to surgically explore the circumflex system for revascularization in patients with severely damaged left ventricles and advanced cardiomegaly. It has also been noted that patients who have to be converted from off-pump to on-pump technique have higher morbidity and mortality risks [Edgerton 2003]. In our study, the frequency of distal anastomoses was high and circumflex system anastomoses were frequent.

Previous work has shown that on-pump non-cardiopulmonary methods are safe and effective in CABG [Akins 1992, Bonchek 1992]. Antunes et al [1999] investigated the use of intermittent aortic cross-clamping (initial 17 patients) and ventricular fibrillation (remaining 90 patients) in the CPB technique for patients with severe LV dysfunction. Their results revealed good myocardial protection and a favorable outcome with both methods. A different study by the same authors reported medium- to long-term survival in this high-risk group of patients [Antunes 2003]. However, intermittent cross-clamping as compared to the other methods, carries higher risk of cerebrovascular complications originating from atherosclerosis in the ascending aorta, a problem that is common in cases of severe LV dysfunction. With the ventricular fibrillation technique, the potential problems of inadequate LV coronary flow and distribution, subendocardial ischemia, and increased myocardial wall tension during surgery are well documented [Buckberg 1975]. Perrault et al [1997] investigated the on-pump-supported, non-cross-clamped beating-heart technique in a group of patients that included some with LV dysfunction (18 cases). They concluded that this technique is an acceptable alternative for high-risk patients. It was also pointed out as an alternative safe procedure for unstable patients [Edgerton 2004].

The primary cause of mortality after repair of an LV aneurysm is low cardiac output. This occurs due to insufficient protection of the myocardium, incomplete myocardial revascularization, and improper reduction of LV volume. There are several advantages to performing LV aneurysm repair on the beating heart in cases of severe LV dysfunction: (1) ischemic damage to the myocardium is minimized; (2) the junction of the scar and normal myocardium can be clearly identified for proper placement of the Fontan stitch; and (3) the surgeon can more accurately judge the required tension on the Fontan stitch (since the heart continues to beat), assess whether a patch is necessary, and, if necessary, determine the size of the patch that will allow optimal LV cavity size.

In cases of LV dysfunction, the long-term outcome with mitral valve repair is better than that with valve replacement [Enriquez-Sarano 1995]. Giunti et al found that patients with impaired LV function and ischemic mitral valve regurgitation could be managed using the on-pump/beating-heart technique via the left atrium with an acceptable postoperative outcome [Prifti 2003]. Alfieri and Maisano introduced edge-to-edge repair, which is performed via ventriculotomy and is an alternative method for patients with LV aneurysm associated with mitral insufficiency [Alfieri 1999]. We opted to use this technique in our two cases of mitral insufficiency because of the ease of accessing the mitral valve through the aneurysmectomy incision, and because it shortened CPB time, which is very important in patients with severe LV dysfunction. Follow-up echocardiography in these two patients showed grade 1 and grade 2 residual mitral regurgitation.

We found that on-pump/beating-heart CABG had no adverse effects on postoperative outcome (Table 4). The frequencies of inotrope usage and intraaortic balloon pump usage were low, even though 24 aneurysmectomies were performed in the study group. Postoperative new onset MI was detected only in two cases. High levels of CK-MB in two patients were performed at our center. The mortality rate was 4.3%. In the literature, the range of hospital mortality noted for patients with severe LV dysfunction who have undergone on- and off-pump CABG is 2.8% to 13.5% [Antunes 1999, Ascione 2003, Goldstein 2003, Meharwal 2002, Moshkovits 1997]. The hospital mortality rate in our study was not different from previously reported rates for severe LV dysfunction. During the same time period in which we conducted this study (March 2001 to March 2004), 1057 other isolated CABG or CABG-associated procedures were performed at our center. The mortality rate for these patients was 1.3%.

On-pump/beating-heart CABG has numerous advantages when compared to off-pump or on-pump cardiopulmonary arrest techniques: (1) sudden cardiac failure due to positional hypotension (which is especially a high risk at the time of circumflex anastomoses) in the off-pump technique is avoided because the circulation is directed by the pump; (2) there is less global myocardial ischemia than occurs with cardiopulmonary arrest; (3) regional ischemia is minimized because the oxygen supply/demand ratio in the revascularization area is reduced (opposite to what occurs with the off-pump technique in intervals of ischemia during anastomosis); (4) detrimental effects of periods of ischemia-reperfusion on the myocardium are alleviated by resting the heart through assisted circulation
during cardiopulmonary bypass when compared to the off-pump technique; (5) LV aneurysm repair can be done in association with CABG; and (6) by applying the side clamp to the aorta only once, all proximal anastomoses can be performed after all distal anastomoses are completed. The latter differs from the off-pump technique, in which hemodynamic stability is best maintained if proximal anastomosis is performed first or immediately after the completion of distal anastomosis in each vessel.

Regardless of the sophistication of the cardioplastic methods used, a certain period of time is always needed to allow the myocardium to recover after potassium blood cardioplegia and cross-clamp removal [Rao 2001]. However, this phenomenon raises the question of whether the currently available myocardial protection methods are ideal or not. In all our cases, we stopped CPB as soon as the proximal anastomoses were completed. On the other hand, in our clinical experience, when the cases who had severe LV dysfunction were operated upon with CPB and cross-clamp technique, assisted circulation was needed for a time period of 5-10 minutes after cross-clamp removal.

In conclusion, on-pump/beating-heart CABG is safe for patients with severely depressed LV function. The on-pump/beating-heart technique offers surgeons the advantages of being able to perform intracavitary procedures and complete revascularization without technical or hemodynamic difficulties. These benefits suggest that on-pump CABG should be the method used in cases of severe LV dysfunction, especially if the patient has an LV aneurysm as well.

REFERENCES


This paper by Gulcan and associates summarizes several important points that apply directly to modern advances in cardiac surgery technique. Whereas cardiac surgery was based exclusively on cardioplegic arrest for over 2 decades, there are now a multitude of techniques and variations. Off-pump beating heart surgery, or OPCAB, is now popular in many centers as it eliminates some of the consequences and costs of the cardiopulmonary bypass circuit. Gulcan et al. presents a series of patients where the pump is used as a biventricular support device, permitting beating-heart techniques to be applied to the empty, resting myocardium. They are correct when they state in their discussion that off-pump techniques cause regional ischemia. This is typically underestimated in the literature and by practicing surgeons. However, the effects of clamping the coronary artery in a fully-loaded, working, beating-heart preparation is clearly a classic model of regional ischemia. Since patients with clinical coronary artery disease often have collaterals, the impact of the ischemia may be “tolerable” during the period of graft construction. However, the physiology is quite definitely ischemic in nature.

The technique discussed by Gulcan is not new, but is increasing both in popularity and utility. Donald Ross, MD, of Sydney, Australia coined the eponym “BHOP” for this technique (“Beating Heart On Pump”). Gulcan’s paper expands the range of BHOP by including 24 patients who also underwent transventricular repair of the mitral valve or aneurysmectomy in addition to CABG.

What makes BHOP a successful technique in patients with marginal LV function is the physiology. When the heart is unloaded and empty, myocardial work is vastly reduced, even at normothermia. If the procedure can be performed without regional ischemia while at the same time lowering myocardial work, the physiology becomes a model of recovery rather than ischemia. This is why BHOP is different from OPCAB and is more useful in the impaired LV or unstable patient.

I would personally offer some technical differences between my own experience with BHOP and those of Gulcan and associates. Although minor in nature, these concepts are helpful improvements. Firstly, it is often very helpful to cannulate the vena cavae separately using angled venous uptake cannulae into a bifurcated drainage line. Then the size of the heart can be further reduced using caval isolation with encircling tapes. This eliminates overflow past the venous cannula and further decompresses both the left and right heart. When the inferior and superior vena cava are cannulated separately, the heart can be flipped over and tucked under the right hemisternum, without being blocked, by the large stiff dual stage cannula. For large hearts, bicaval cannulation with tapes can make the difference in lateral wall exposure. If the heart is still incompletely drained, a vent through the main pulmonary artery or the superior pulmonary vein can achieve complete decompression.

Secondly, the use of intracoronary shunts provides an additional protection against ischemia. It is now well proven that shunts prevent regional ischemia by eliminating back-bleeding and providing some anterograde flow. In animal and human studies, markers of ischemia are reduced when shunts are used compared with non-shunted cases. Even though the heart is fully decompressed in BHOP, oxygen and metabolic delivery is still important and so I continue to use shunts.

Thirdly, the strategy for top-end reconstruction can be unique and flexible during BHOP. It is my practice to use periods of mini-circulatory arrest at 30°C inflow temperature to construct the top ends without the use of a partial occlusion clamp. After construction of the distal anastomosis, the graft is filled with saline and placed against the ascending aorta. Pump flow is reduced to 500 cc/min and the vein graft is sized, beveled and the first anastomotic stitch placed. The pump is stopped and a single punch hole (or incision) created. Volume is drained into the oxygenator until the blood pool in the top of the aorta just drops below the edge of the aortotomy, permitting suturing under direct vision. Then the venous line is clamped and one-half of the proximal sutures line completed. This usually takes me 3 minutes. Then the pump is started again and blood is allowed to flush out of the proximal anastomosis until it is certain no air remains in the aorta. The surgeon’s finger controls the bleeding while the patient is perfused on full bypass for 3 minutes. The pump is stopped in the same manner while the remaining half of the suture line is completed. De-airing is done by leaving the sutures unsecured until after flow has resumed. This technique has been extremely useful to me in many different BHOP circumstances. The sequence of “bottom then top” is a familiar and efficient surgical flow, and is preserved by using mini-circ arrest during BHOP. I have been able to perform top ends without any aortic clamping at all, avoiding focal aortic plaques and calcifications. No neurologic events have occurred in any patient.

Finally, the costs of combining the pump circuit and beating-heart stabilizers is an issue in some programs. However, re-usable stabilizers are now available and employing these devices levels the costs of BHOP to equal those of a conventional pump case. The BHOP cases usually take longer than equivalent cross-clamped cases, and thus should be reserved for cases where there is potential benefit. Gulcan and associates are to be congratulated in their thorough discussion on the indications, technique, and physiology of this important technique. Every surgeon practicing today should be able to have a smooth transition between OPCAB, BHOP, and cross-clamped techniques at any time, even during the same case if needed.

Mark M. Levinson, MD
Hutchinson Hospital
Hutchinson, Kansas

Note to the Author: There is a callout for a Table 4 (page 4, second column, paragraph 2) but we do not have a table 4. Could you please confirm that you meant to refer to Table 3? Or provide us with a Table 4. Thank you.