Adult Patients who were Breastfed are Less Anxious but Suffer More Frequently of Non-Diarrheic Functional Bowel Disorders

Michel Bouchoucha1,2*, Ghislain Devroede3,4, Pierre Rompteaux2, Florence Mary2, Bakhtiar Bejou2 and Robert Benamouzig2

1Université Paris Descartes, 15 Rue de l’école de Médecine, France
2CEFRED (Centre d’Exploration Fonctionnelle et de Rééducation Digestive), Service de Gastroentérologie, Hôpital Avicenne, France
3Département de Chirurgie, Faculté de Médecine, Université de Sherbrooke, Québec, Canada
4Hôpital Fleurimont (CHUS), 3001 12 Avenue Nord, Sherbrooke, Canada

*Corresponding author: Dr. Michel Bouchoucha, Université Paris Descartes, 15 Rue de l’école de Médecine, 75270, Paris; CEFRED (Centre d’Exploration Fonctionnelle et de Rééducation Digestive), Service de Gastroentérologie, Hôpital Avicenne, 125 Rue de Stalingrad, 93000 Bobigny, France, Tel: 33-148957432, Fax: 33-148957437

Abstract

Introduction: Functional gastrointestinal disorders are pathologies of multifactorial origin. A shorter duration of breastfeeding has been found to enhance the prevalence of irritable bowel syndrome (IBS) in adulthood. The present observational study aims mainly to evaluate if breastfeeding is associated with IBS only or with other functional gastrointestinal disorders (FGIDs).

Patients and methods: 1106 consecutive FGID patients (70% female) aged 48.4 ± 16.6 years (M ± SD), (BMI 26.9 ± 11.0 kg/m²) filled both a Rome III questionnaire, a psychological evaluation and a questionnaire about breastfeeding. The backwards selection procedure was used for model selection during multivariate logistic regression.

Results: Breastfed patients are older (P = 0.039), and have lower state anxiety (P = 0.004; HR = 0.986; 95% CI = [0.976-0.995]). They suffer more frequently of IBS with constipation (P = 0.028; HR = 1.866; 95% CI = [1.069-3.256]), mixed IBS (P = 0.006; HR = 2.181; 95% CI = [1.254-3.792]), functional constipation (P = 0.006; HR = 1.909; 95% CI = [1.199-3.040]), and bloating (P = 0.039; HR = 1.624; 95% CI = [1.026-2.571]). In contrast to esophageal, gastroduodenal and anorectal disorders which were not associated to the fact of having been breastfed or not.

Conclusion: Our results support the presence of an association between breastfeeding and non-diarrheic functional bowel disorders (IBS, IBS with constipation, mixed IBS, functional constipation and bloating) in FGID patients, but it also demonstrates that these people are less acutely anxious.

Keywords

Breastfeeding, Functional gastrointestinal disorders, Irritable bowel syndrome, Depression, Anxiety, Constipation, Bloating

Abbreviations

FGID: Functional Gastrointestinal Disorders; BMI: Body Mass Index; IBS: Irritable Bowel Syndrome

Introduction

Many patients have persistent and recurring GI symptoms attributed to the digestive system. The Rome criteria [1], a classification of the functional gastrointestinal disorders (FGIDs) has been proposed, for FGIDs not associated to any structural or biochemical abnormalities. These disorders can affect any part of the GI tract (esophagus, stomach, colon, terminal intestine). FGIDs are not psychiatric disorders, although stress and psychological difficulties can make FGIDs worse. There are three primary features of FGIDs, namely motility, sensation and brain-gut dysfunction.

The prevalence of FGIDs in the general population is high: Functional dyspepsia 20 to 30%, Irritable Bowel Syndrome (IBS) 10 to 20%, functional constipation up to 27%, pelvic floor dysfunction 5 to 11% [2]. More than...
half of subjects with FGID symptoms do not consult a physician, and take over-the-counter medications. These subjects also report significantly more job absenteeism and disability than healthy people [3]. Thus the high prevalence of a relatively benign problem is costly [4], those afflicted report power quality of life [5] and the search of a basic reason to these common dysfunctions remains very much in order [6,7].

It has long been known that breastfed children are more resistant to infections (gastroenteritis, ear infections, etc.) than others [8]. This effect is linked to several immunological and non-immunological mechanisms. Secretory immunoglobulin (IgA, IgG and IgM), absent from the intestinal cells of newborn infants [9,10], intact immune cells (B and T lymphocytes, macrophages, leucocytes) as well as immunity-stimulating factors [11,12] and non-immunological factors [13] can be found in the mother’s milk. Recent studies have shown that nutrition has a major impact on early microbiota composition until cessation of breast-feeding, and is necessary for their maturation into adult-like microbiota [14].

A recent study concluded that early environmental factors may play a role in the subsequent genesis of IBS [15]. The authors investigated 767 Australian subjects, and searched for the presence or not of IBS excluding organic diseases simply on the basis of self-reported rather than clinical investigation. They found that development of IBS was associated with childhood factors namely a shorter duration of breastfeeding, sharing a bedroom, exposure to herbivore pets and hygiene factors. Overall, they were extremely careful in their conclusions, wishing to rule out a type I error. They also investigated patients with functional dyspepsia, but they found no association with breastfeeding.

The aim of the present study was to evaluate if breastfeeding is associated with mood disorders and specific functional gastrointestinal disorders.

### Patients and Methods

#### Subjects

From January 1, 2011 to December 31, 2014, 1205 outpatients were consecutively referred by gastroenterologists to our Center for Functional GI and Motility Disorders (CEFRED) (Centre d’Exploration Fonctionnelle et de Rééducation Digestive, Gastroenterology Clinic of the Avicenne Hospital), a tertiary center for FGID management. Among them, only 99 (9%) were unable to specify whether or not they were breastfed, and excluded for this reason. The 1106 remaining patients with a full data set are included in the present study.

Before inclusion, a full evaluation had failed to yield any organic cause for the patients’ complaint, although they were screened for bacterial overgrowth, eosinophilic colitis and connective tissue disorders. They also had morphological evaluation (endoscopy or radiology). Metabolic, endocrinologic, neurologic and psychiatric etiologies were excluded. Patients with drug addictions or previous digestive surgery, except cholecystectomy and appendectomy, were causes of exclusion from the study. A single investigator (MB) confirmed independently, during the medical visit, the validity of the initial diagnosis of FGID, and of all data mentioned above.

The study was declared in the French National Agency for drug safety (ANSM, Agence Nationale de Sécurité du Médicament et des produits de santé, decision number: 2015-A00954-45) and conducted according to the Declaration of Helsinki and Good Clinical Practice (GCP) guidelines.

### Experimental Procedure

#### Study design

The comparison of the groups of FGID patients was performed within the framework of an observational study.

#### Rome III questionnaire

Patients in the gastroenterologist’s office (MB) filled out a standard clinical questionnaire based on Rome III questionnaire [16]. The diagnostic process was previously described in published studies [17-19]. Functional esophageal disorders (heartburn, chest pain of presumed esophageal origin, dysphagia and globus) [20], functional gastroduodenal disorders (dyspepsia, post-prandial distress syndrome, epigastric pain syndrome, belching disorders, aerophagia, unspecified excessive belching, nausea with or without, vomiting disorders, and rumination syndrome) [21], functional bowel disorders (Irritable bowel syndrome (IBS) and its subtypes (IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), mixed IBS (IBS-M) and unsubtypeed IBS (IBS-U), bloating, constipation, diarrhea, and unspecified) [1], abdominal pain syndrome [22], and anorectal disorders (fecal incontinence, functional anorectal pain, including levator ani syndrome and Proctalgia fugax, difficult defecation) [23], were diagnosed according to Rome III criteria. In addition regurgitation, soiling, and stool description using Bristol Stool Form Scale [1] were also recorded.

Finally, a question about breastfeeding (“Were you breastfed?” Answer “Yes” or “No”; not otherwise specified) was asked to all patients. This question has been asked all along because of the long known debate among pediatricians on a possible relationship between breastfeeding and constipation in babies [24,25].

### Psychometric evaluation

Psychometric evaluation was focused on anxiety and depression. The level of depression was assessed by the French validated translation of the Beck Depression Inventory (BDI II) [26], frequently used in the evaluation of depression in gastrointestinal pathologies [19,27].
Logistic regression was used for data analysis, systematically including age, gender, body mass index (BMI), depression, state and trait anxiety, functional gastrointestinal disorders as independent variables, and breastfeeding as dependent variable. The backwards selection procedure was used for model selection during multivariate logistic regression. Statistically significant variables (P < 0.05) remained in the adjusted model.

**Results**

There was a female predominance (70% female) in the population studied (Table 1). Patients had a mean age of 48.4 ± 16.6 years, and a BMI 26.9 ± 11.0 kg/m². The mean duration of the symptoms was 12 ± 10 years (range 1 to 36 years).

**Table 1: Demographics and clinical description of the population. Quantitative variables are expressed as mean ± standard deviation and qualitative variables are expressed as number (percentage).**

<table>
<thead>
<tr>
<th></th>
<th>All subjects</th>
<th>Breastfeeding</th>
<th>No breastfeeding</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>N</td>
<td>1,106 (100)</td>
<td>454 (41)</td>
<td>652 (59)</td>
<td></td>
</tr>
<tr>
<td>Female patients</td>
<td>778 (70)</td>
<td>330 (73)</td>
<td>448 (69)</td>
<td>0.087</td>
</tr>
<tr>
<td>Age (years)</td>
<td>48.4 ± 16.6</td>
<td>47.2 ± 17.0</td>
<td>49.3 ± 16.2</td>
<td>0.039</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>26.9 ± 11.0</td>
<td>27.5 ± 6.3</td>
<td>26.5 ± 13.3</td>
<td>0.140</td>
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<tr>
<td><strong>Psychological</strong></td>
<td></td>
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<tr>
<td>Depression</td>
<td>11.9 ± 10.0</td>
<td>11.5 ± 9.4</td>
<td>12.2 ± 10.4</td>
<td>0.284</td>
</tr>
<tr>
<td>State anxiety</td>
<td>39.9 ± 12.8</td>
<td>38.6 ± 12.6</td>
<td>40.7 ± 12.9</td>
<td>0.008</td>
</tr>
<tr>
<td>Trait anxiety</td>
<td>42.4 ± 10.8</td>
<td>41.8 ± 10.5</td>
<td>42.8 ± 11.1</td>
<td>0.125</td>
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<tr>
<td><strong>Gastroesophageal</strong></td>
<td></td>
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<tr>
<td>Globus</td>
<td>219 (20)</td>
<td>82 (18)</td>
<td>137 (21)</td>
<td>0.128</td>
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<tr>
<td>Regurgitation</td>
<td>145 (13)</td>
<td>50 (11)</td>
<td>95 (15)</td>
<td>0.051</td>
</tr>
<tr>
<td>Heartburn</td>
<td>303 (27)</td>
<td>117 (26)</td>
<td>186 (29)</td>
<td>0.173</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>363 (33)</td>
<td>140 (31)</td>
<td>223 (34)</td>
<td>0.134</td>
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<tr>
<td><strong>Gastroduodenal</strong></td>
<td></td>
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<tr>
<td>Epigastric pain</td>
<td>84 (8)</td>
<td>27 (6)</td>
<td>57 (9)</td>
<td>0.052</td>
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<tr>
<td>Postprandial distress</td>
<td>199 (18)</td>
<td>86 (19)</td>
<td>113 (17)</td>
<td>0.271</td>
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<tr>
<td>Dyspepsia</td>
<td>267 (24)</td>
<td>100 (22)</td>
<td>167 (26)</td>
<td>0.097</td>
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<tr>
<td>Aerophagia</td>
<td>286 (26)</td>
<td>112 (25)</td>
<td>174 (27)</td>
<td>0.247</td>
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<tr>
<td><strong>Bowel</strong></td>
<td></td>
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<tr>
<td>IBS (all subtypes)</td>
<td>365 (33)</td>
<td>160 (35)</td>
<td>205 (31)</td>
<td>0.104</td>
</tr>
<tr>
<td>IBS-Constipation</td>
<td>54 (5)</td>
<td>28 (6)</td>
<td>26 (4)</td>
<td>0.066</td>
</tr>
<tr>
<td>IBS-Diarrhea</td>
<td>67 (6)</td>
<td>21 (5)</td>
<td>46 (7)</td>
<td>0.061</td>
</tr>
<tr>
<td>IBS-Mixed</td>
<td>56 (5)</td>
<td>30 (7)</td>
<td>26 (4)</td>
<td>0.036</td>
</tr>
<tr>
<td>IBS Unspecified</td>
<td>109 (10)</td>
<td>33 (7)</td>
<td>76 (12)</td>
<td>0.010</td>
</tr>
<tr>
<td>Constipation</td>
<td>80 (7)</td>
<td>43 (9)</td>
<td>37 (6)</td>
<td>0.012</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>194 (18)</td>
<td>81 (18)</td>
<td>113 (17)</td>
<td>0.444</td>
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<tr>
<td>Bloating</td>
<td>83 (8)</td>
<td>41 (9)</td>
<td>42 (6)</td>
<td>0.069</td>
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<tr>
<td><strong>Abdominal pain</strong></td>
<td></td>
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<tr>
<td>Soiling</td>
<td>122 (11)</td>
<td>49 (11)</td>
<td>73 (11)</td>
<td>0.457</td>
</tr>
<tr>
<td>Fecal Incontinence</td>
<td>96 (9)</td>
<td>34 (7)</td>
<td>62 (10)</td>
<td>0.143</td>
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<tr>
<td>Levator ani syndrome</td>
<td>87 (8)</td>
<td>39 (9)</td>
<td>48 (7)</td>
<td>0.262</td>
</tr>
<tr>
<td>Levator ani syndrome</td>
<td>69 (6)</td>
<td>27 (6)</td>
<td>42 (6)</td>
<td>0.420</td>
</tr>
<tr>
<td>Proctalgia fugax</td>
<td>58 (5)</td>
<td>21 (5)</td>
<td>37 (6)</td>
<td>0.265</td>
</tr>
<tr>
<td>Non specific</td>
<td>59 (5)</td>
<td>25 (6)</td>
<td>34 (5)</td>
<td>0.467</td>
</tr>
<tr>
<td>Defecation disorders</td>
<td>372 (34)</td>
<td>154 (34)</td>
<td>218 (33)</td>
<td>0.458</td>
</tr>
<tr>
<td><strong>Bristol stool form</strong></td>
<td>3.8 ± 1.9</td>
<td>3.8 ± 1.9</td>
<td>3.7 ± 1.8</td>
<td>0.608</td>
</tr>
</tbody>
</table>

IBS: Irritable Bowel Syndrome.
**Univariate analysis**

The patients who were breastfed were fewer than those who were not (41% vs. 59%; p < 0.001), but younger (P = 0.039). The BMI and the proportion of female patients are not different in breastfed and non-breastfed patients.

Among psychological parameters, state anxiety is lower in breastfed patients (38.6 ± 12.6 vs. 40.7 ± 12.9; P = 0.008), whereas depression and trait anxiety are comparable in the two populations (Table 1).

Breastfed patients complain less frequently of dysphagia (P = 0.011), but the complaint of other esophageal disorders and gastroduodenal disorders are similar in the two groups (Table 1). Among bowel disorders, breastfed patients have more frequently mixed IBS (P = 0.010), unspecified IBS (P = 0.012), and functional constipation (P = 0.016). Among the other functional bowel disorders, IBS with constipation (P = 0.066), IBS with diarrhea (P = 0.061), and bloating (P = 0.069) show non-significant increase in breastfed patients (Table 1). The frequencies of anorectal disorders are also comparable in breastfed and non-breastfed patients.

**Multivariata analysis**

The multivariate analysis confirmed the positive association of breastfeeding with state anxiety (P = 0.004; HR = 0.986; 95% CI = [0.976-0.995]), IBS with constipation (P = 0.028; HR = 1.866; 95% CI = [1.069-3.256]), mixed IBS (P = 0.006; HR = 2.181; 95% CI = [1.254-3.792]), functional constipation (P = 0.006; HR = 1.909; 95% CI = [1.199-3.040]), and bloating (P = 0.039; HR = 1.624; 95% CI = [1.026-2.571]).

**Discussion**

The present study demonstrates that patients who were breastfed are less anxious, but also have increased odds of presenting specific functional bowel disorders with delayed transit: IBS with constipation, mixed IBS, and functional constipation as well as bloating, while pathologies with shorter transit, i.e. diarrhea, IBS with diarrhea, upper FGIDs (esophageal, gastro-duodenal) and anorectal disorders are not associated to breastfeeding.

Breastfeeding does not protect against diarrhea, and favors delayed transit: Odds of constipation and odds of IBS with constipation are 1.9 fold increased. Yet, Bristol stool form was not different between breastfed and non-breastfed patients. Pediatricians often incriminate breastfeeding in the genesis of constipation in babies [24]. In this study, the increased odds of bloating (3.5) could be interpreted as a result of the delayed transit. Indeed, previous studies have shown the importance of methanol production in constipated subjects [32-34]. In the present study, the methane production was not evaluated and further studies are needed to evaluate. In contrast, many studies on the importance of the microbiota on FGIDs tend to enhance the importance of environmental factors [35-38].

Recent data have shown that childhood environment factors, particularly bedroom sharing and pet exposure are a risk factor for IBS in later life [15]. These authors also found that a shorter duration of breastfeeding was significantly associated with IBS as an adult, but they failed to identify the subtypes of IBS, such as defined by the Rome III group, thus lumping together patients with constipation and those with diarrhea, although these are clearly different psychologically [19,39] and in terms of pathophysiology. Moreover, they also failed to recognize the fact that patients may evolve from functional constipation to IBS with constipation or vice-versa [40]. It is possible that behind these reasonably objective considerations on the importance, role and impact of breastfeeding, in terms of future digestive function, as part of modality of expression, there are much more basic different attitudes toward real or not difference between the old fashioned “biomedical” model of health and disease, and the more contemporaneous “biopsychosocial” model of medicine [41]. In short, that is the key question in all these studies including the present one.

Taking into account all possible variables including caring and maternal attitude [42], different elements may be at work during breast feeding, namely type of delivery, quality and type of maternal milk [43], its impact on the intestinal flora of the newborn baby [44], immunity as well as duration of breastfeeding [15], and use of antibiotics, etc. One must also consider all variables at work only after birth in view of mother-child attachment. Simply said, at the beginning of life, babies only have their body to speak out, and visceral somatization conceivably could be part of the process.

There are several methodological limits to the present study even if it confirms with a much larger group of patients, the study which demonstrated that environmental factors may play a role in the future occurrence –or genesis–of FGIDs [15], indeed, it does not take into account duration of breastfeeding, and changes in maturation of the baby’s intestine over the first months of life. A second limit is the impossibility to assess the validity of a past history of breast feeding in adult patients. This limit was the same in previous published studies [15]. This objection could have been lifted by mother’s interviews. Another limit is the absence of a healthy control group in the present study. However, it would be impossible to recruit two control cohorts of babies which are breastfed or not, follow them over decades and evaluate them subsequently for FGIDs, on the basis of the Rome criteria, established only in 2006, and make sure they do not have an underlying organic disease masked clinically as a gut dysfunction. One might also argue to have as
basis of study a group of healthy subjects not suffer-
ning from FGID, referred according to a rigid algorithm
defining the different types of FGID, and eliminating
those not scoring positive for the Rome III criteria.
Finally the question used didn’t take into account
the duration of breastfeeding [45], that could interact
with the intestinal microbiota [46].

The previous study [15] investigating the poten-
tial influence of breastfeeding on future occurrence
of FGIDs is entirely speculative when addressing the
question of “hygiene hypothesis”. We don’t have
data to support or not such hypothesis.

Breast-fed newborns have been demonstrated to
carry a more stable and uniform microbiota population
when compared to the formula-fed ones [47]. Breast
milk can participate in the bacterial colonization of the
breast-fed newborn [48]. The newborn is then contin-
uously exposed to new bacteria from the environment,
food and skin bacteria from adults via feedings, petting
or kisses. Once dietary supplementation begins, mi-
icrobiota profile of breast-fed infants changes and be-
tween the first and the second year of life, differences
between breast- and formula-fed infants are lost [49].
In addition, it was shown that breastfed could change
the distribution of intestinal cells of Cajal in the small
intestine and in the colon of a rodent model [50], and
then alter the transit.

Another important aspect of breastfeeding is its
psychological consequence for the mother as well
as for the newborn. These become less anxious if
breastfed. For the mother, postpartum depression is
predicted by breastfeeding cessation and associated
with shorter breastfeeding duration [51]. On the oth-
er hand, providing breast milk symbolizes embodied
contact with their baby and increases maternal con-
fidence [52]. All subjective and emotional exchange
that may or not may occur between mother and child
at that time, including all olfactive and gustative ele-
ments experienced by the baby. May carry an impact
still visible during adulthood. It is not known if the
psychosomatic separation or even dissociation has an
impact on bowel function. It may possibly shed some
light why a severe deleterious trauma such as sexual
abuse, is found more often in the past history of pa-
tients with lower gastrointestinal dysfunction rather
than in those with upper gastrointestinal dysfunction [53].

This study was performed in a tertiary center
where patients consult for management of FGIDs,
and are not a part of the general population. 99 pa-
tients were unable to indicate whether or not they
were breastfed, but the high significance of our re-
results allows to eliminate reasonably this parameter as
a key factor. On the other hand, the relatively small
number of breastfed patients (41%) is lower than the
actual frequency of breastfed subjects (74%) in
France [45]. However, the frequency of breastfeeding
found in the present study is in agreement with the
mean age of the patients.

To conclude, breastfed patients suffered more from
IBS-C, IBS-M, FC, and bloating and had lower “state”
anxiety. In contrast, breastfeeding was not associated
with esophageal, gastro-duodenal orano-rectal disor-
ders. These results must be confirmed by further pro-
spective studies.

Authorship Statement

MB: Performed the research, contributed to the
design of the study, performed data analysis, partic-
ipated in the interpretation of data, wrote the arti-
cle, revised the article for its content, and approved
its final version; GD: Revised the article for its con-
tent and approved its final version; PR: Participated
in the selection of the patients and revised the article
for its content; FM: Participated in the selection of
the patients and revised the article for its content;
BB: Participated in the selection of the patients and
revised the article for its content; RB: Participated in
the selection of the patients, contributed in the de-
sign of the study, revised the article’s content and
gave final approval for the version to be published.

Competing Interests

Michel Bouchoucha, Ghislain Devroede, Florence
Mary, Pierre Rompeaux, Bakhtiar Bejou, Robert Ben-
amouzig have no competitive interests.

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Ethics

The study was conducted in accordance with the
Helsinki Declaration and was approved by the local
medical ethics reviews board. Written informed con-
sent was obtained from all patients.

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