Outcomes in adulthood of gastric transposition for oesophageal atresia

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Abstract

Background: Long term outcomes of gastric transposition (GT) for complex oesophageal atresia (OA) are poorly reported. We aimed to perform comprehensive long term follow up of adults who had been treated with GT for OA as children.

Methods: Consecutive patients who underwent GT for OA in childhood aged > 18 years old were identified alongside age matched patients who had primary repair (PR). Type of OA, co-morbidities and details of surgery were recorded. Telephone interviews included medical history, current symptoms - including gastrointestinal symptom rating scale (GSRS), morbidity and health related quality of life (HRQoL) using gastrointestinal quality of life index (GIQLI).

Results: 32 participants were interviewed in each group (mean age 29 years). BMI (19.9 ± 3.5) was significantly lower (p=0.0006) in GT group. 6/32 (19%) still required supplementary feeding. Adult morbidity included anastomotic stricture (34%), chronic respiratory disease (28%), dumping symptoms (25%), anaemia (47%) and depression (19%). 3 patients required major revision surgery.

Participants in both groups report regular upper gastrointestinal symptoms (GSRS: GT = 2.1, PR = 2.0) and were more symptomatic than the normal population (1.4) but not statistically different from each other. HRQoL (GIQLI = 113) was lower than after PR (122) but not significantly different (p=0.29) and the normal population (125). 23% of GT participants had higher than normal HRQoL.

Conclusions: GT for OA is associated with significant morbidity and symptoms, including issues previously unreported in adulthood such as mental health problems. This mandates long term follow up and quality transition of these patients into adult care.
Introduction

Oesophageal replacement may be required in cases of oesophageal atresia (OA) where a ‘long gap’ is present or following complicated primary surgery. Gastric transposition (GT) is one such method for replacing the oesophagus and was popularised in the paediatric population by Spitz [1] at our institution in the 1980s and has become the operation of choice in the UK and Europe [2].

As with many of the congenital conditions we have good understanding of the short and medium-term outcomes in childhood following GT. Perioperative morbidity such as leak, reoperation and stricture rates are well reported and acceptable in comparison to other forms of oesophageal replacement [3-6]. Longer term morbidity such as delayed gastric emptying, dumping syndrome and poor weight gain are also well reported and despite this most authors report good functional outcomes following GT in childhood [3, 4, 7, 8].

However as increasing numbers of patients who had GT for OA move into adulthood our knowledge of their truly long-term outcomes is poor. GT is used in adults principally as a conduit after oesophagectomy for cancer in a more elderly population. Morbidity such as reflux, dysphagia and dumping syndrome are reported but quality long term outcome data are limited, making extrapolation of this limited data to the very different congenital OA population of limited value [9].

Whilst detailed follow-up into adulthood of uncomplicated OA has increasingly been reported [10-13], similar work for GT, or other oesophageal replacement methods such as colonic or jejunal interposition, remains limited due to the rarity of oesophageal replacement, poor long term clinical follow up and inconsistent transition of care to adult services. Those few studies that do include adult outcomes of GT are limited to single outcomes such as quality of life [14], or report outcomes of mixed cohorts of children plus small numbers of adults [5].

Our aim was therefore to perform a comprehensive long term follow up study of adult patients who had been treated with GT for OA as children, including morbidity, symptoms, functional outcomes and quality of life. We also aimed to study an age matched group of uncomplicated OA who underwent primary repair (PR) during the same time period, managed by the same surgeons in order to have a reference point other than the normal population to compare data with and give context to the results.
Methods

The study was given National Research Ethics Service approval (REC reference: 15/LO/1325). Existing hospital oesophageal atresia databases were used to identify consecutive patients who had undergone GT for OA and were over 18 years of age at the time of the study. Only UK based patients were included. A comparative age matched group of patients who had undergone primary repair (PR) of uncomplicated OA was also identified. These patients were aged matched by selecting patients from existing databases who had repair over the same time period as the GT cohort. More formal individual patient matching was considered but felt not possible due to the limited number of cases available and large numbers of co-morbidities in both groups which would make matching very difficult to control.

Potential participants were initially sent postal invitations to take part in the study and a subsequent telephone follow up was used to confirm interest in the study, arrange written consent and schedule a telephone interview.

Telephone interviews were all conducted by the same paediatric surgeon (EH) and involved: confirmation of demographics, detail of type of OA and associated anomalies, full medical and surgical history – in childhood and adulthood, current symptoms and morbidity, and completion of questionnaires. Details of OA, operative history, associated anomalies and paediatric history were confirmed from available clinical notes and hospital databases.

The two validated questionnaires used were the gastrointestinal symptom rating scale (GSRS) and gastrointestinal quality of life index (GIQLI). GSRS is a tool validated for the assessment of disease specific gastrointestinal symptoms. It is made up of 15 questions, answered using a 7 point Likert scale [15]. Questions can be grouped into sub-scales for abdominal pain, reflux, indigestion, constipation and diarrhoea. Total scores are calculated from the mean scores across each scale and the higher the score the more symptomatic the patient. The GSRS has been validated for use in English, in interview or written format and has been shown to be reliable and valid when assessing adults with upper gastrointestinal and reflux symptoms hence its selection for this [16]. Normal values have also been published in a European adult population [17]. GIQLI is a 36-question health related quality of life score specifically designed for adult gastrointestinal disease[18]. Results can be assessed as a total score or within more specific domains including symptoms, social, physical, and emotional quality of life. Whilst designed and validated in Germany it was also translated and tested in English language. It has been used for many different types of upper gastro-intestinal conditions including benign disease such as following cholecystectomy and in malignancy, including assessment of patients with oesophageal cancer after gastric conduit reconstruction. It has also been used to assess medium and long term HRQoL in oesophageal atresia patients including those with complex disease requiring replacement surgery. Data for GIQLI and GSRS were scored and collected as described in the original literature [15,18].

Statistical analysis was performed using GraphPad Prism® 8.0.2. Data are presented as median and IQR unless otherwise stated and non-parametric tests were used (Mann Whitney U) to compare groups (GIQLI / GSRS) as data did not follow a normal distribution.
Results

Recruitment

Over the time period 231 patients underwent GT in our centre, of whom 117 had undergone GT for oesophageal atresia. Of these, 61 were international/private patients who we did not have ethical approval to contact. Fifty-six NHS patients are now adults over 18 years, of whom UK contact details could be traced for 44 who were sent postal invitations. Thirty-two of these were interviewed, representing 73\% of those sent invitations, and 57\% of the entire UK cohort. A recruitment flow chart for GT patients is shown in Figure 1. Thirty-two adults who had undergone PR were also recruited. Two individuals in each group suffering from learning and/or communication difficulties had interviews performed via a proxy or carer. These individuals could not complete the validated questionnaires, but the interviews were included to minimise selection bias. Therefore, data from 32 GT and 32 PR interviews were analysed and 30 in each group for validated questionnaires. 61 overseas patients were not included in the study due to the practical difficulty and language limitation of contacting these patients. Paediatric mortality in complete cohort of 117 was 5 cases (3.8\%).

Demographics and patient characteristics

Demographics, type of OA and associated abnormalities are shown in Table 1. GT and PR participants had a similar age and gender distribution. The presence of any associated congenital abnormality was the same in each group, although renal anomalies were more frequent in GT. One PR and 2 GT participants had required renal transplants as a result of renal anomalies.

56\% of GT patients had primary surgery – defined as the gastric transposition being performed as the first definitive repair of long gap OA, whereas secondary surgery was performed as rescue surgery following failed primary repair or in 2 patients following failed colonic interposition. 81\% of both groups were employed (this included mothers at home caring for children independently) although more GT participants were employed on a part time basis.

Interview-reported symptoms and outcomes

GT participants experienced more morbidity and chronic disease in adulthood than PR participants. BMI was significantly lower in GT participants than in those who had PR (p<0.0006). Accordingly, supplementary jejunostomy feeding was still required in adulthood in six (13\%) participants. Of these, one participant had an unsafe swallow following a road traffic accident mandating jejunal feeding. Three participants needed a jejunostomy due to significant respiratory disease limiting oral intake; one had a history of laryngeal cleft limiting oral intake, and two recurrent aspiration and lung disease. The other two participants were jejunally fed due to severe dumping syndrome and recalcitrant poor gastric emptying. The median BMI in those patients needing supplementary feeding was 19.2 (range 14.9 - 27.1).

Although symptoms suggestive of dumping syndrome were described by 8 (25\%) GT participants, only 6 (16\%) reported having a formal diagnosis of dumping syndrome. Major revision surgery was reported by 3 GT participants. Detailed notes of the revision surgery were not available but were reported to include a partial gastrectomy and jejunostomy, and replacement of gastric transposition with a colonic interposition. The third revision surgery participant could not recall the procedure but involved a Roux-en-Y reconstruction.

Anastomotic dilatations were reported in more than a third of GT participants (34\%) versus 13\% of PR participants. This included one participant who performs regular bougie self-dilatation of a
complex anastomotic stricture at home. Although numbers of participants with chronic respiratory disease was similar between the two groups, 3 GT patients had severe chronic respiratory disease such as bronchiectasis and were under the care of respiratory hospital physicians. Anaemia was the most commonly reported morbidity. Whilst most participants did not know specific details of their anaemia, 3 reported upper gastrointestinal bleeding and ulceration requiring endoscopy. The frequency of gastrointestinal and respiratory symptoms is shown in Figure 2.

GSRS and GIQLI scores

The total GSRS score appeared to be higher (i.e. worse) than age matched normal controls [17] in both the GT and PR groups (Figure 3) with the median and 95% CI of participants above the 95% CI of the mean of the normal controls, although this could not be formally statistically evaluated without the raw data for the controls. For the sub-scales (Figure 4), median scores for indigestion and reflux were above the 95% CI for the controls in both the GT and the PR groups, above the 95% CI for the controls for diarrhoea in the GT group but not the PR group, and above the 95% CI for the controls for constipation in the PR group but not the GT group; there was no significant difference between the GT and PR group for any of the subscales.

Gastrointestinal quality of life (GIQLI) scores are shown in Figure 5. The GT group had lower median quality of life with median GIQLI score of 113 (95% CI 102-122) compared with the PR group with a score of 122 (101-128) which was similar to the normal population figure of 125 [18]. Although the quality of life score was higher in the PR participants, this was not significantly different from the GT group (p=0.29). Statistical comparison to normal population data was not possible due to a lack of the normal population raw data. Despite the median score being lower than the normal population mean, 7 (23%) GT participants had a higher i.e. better quality of life score than the normal population mean. There was no statistical difference between groups for different domains of GIQLI – symptoms, physical, social and emotional quality of life.
Discussion

Data on long term outcomes of GT are sparse, especially in adulthood, and this study goes some way to fill that gap in understanding. We demonstrate an important burden of symptoms, morbidity and reduced HRQoL suffered by these patients as adults. The PR group who we already know suffer morbidity into adulthood [10, 12, 19] also provide some context within which the results of GT can be considered, although are not a truly comparable group.

Due to the rare nature of paediatric GT current literature is limited to retrospective series[3, 7, 8, 20, 21] and reviews or metanalysis[4, 6, 20] of such series. The detail, quality and duration of follow up in these papers is variable and the definition of ‘long term’ follow up in some needs questioning. Loukogeorgakis et al’s [4] review of oesophageal replacement methods in OA used 1 year as representing ‘long term’ follow up. Gallo et al’s [6] meta-analysis of replacement techniques quoted a range of 0.5 – 41 years whilst their comparison of GT and jejunal interposition had median follow up of just 14 years [22]. More recently Awad et al presented morbidity in a small series of GT patients with median follow up of 8.5 years [20] and a literature review of papers with follow up of only 5 years. The mean follow up of this study (29 years) is one of the longest in the literature and given the coverage of morbidity, symptoms and health related quality life makes it the most comprehensive.

The most frequently reported outcomes of oesophageal replacement for OA are peri-operative e.g anastomotic leak, surgical complications and strictures [4, 6]. Longer term GT outcomes which have been commonly reported include feeding issues such as reflux, dumping syndrome, delayed gastric emptying and jejunostomy problems [6, 20, 22]. Other reported morbidity in childhood includes poor weight gain and anaemia [20, 23, 24]. Our results confirm that much of the morbidity reported is not isolated to childhood.

GT affects nutritional status into adulthood. Whilst the mean BMI for GT participants was ‘normal’ at 21 (+/- 3.5) it was significantly lower than in PR participants and 12/32 participants were classed as underweight (BMI <18.5). There are poor comparative data for nutritional outcomes after GT.

Davenport et al looked at 16 early patients, 9 years post GT (including some patients from the same cohort as this study) who had GT in infancy and found 11/16 patients had weight between the 3rd and 97th centile for age [23]. Gallo et al found 44% of GT patients to have an SDS weight/age of less than -2 and Spitz described mean BMI being around the 25th centile for age reviewing his series in 2009 [16, 22, 25]. Long term outcomes in larger OA population studies including all OA types have shown normal mean BMIs [26] and describing catch up growth in OA patients through infancy and childhood [12].

There are several reasons identified that potentially explain why GT participants have a lower BMI than the PR group. Supplementary feeding was still required into adulthood in 6 (19%) participants for a variety of reasons. Ng et al [27] report 37% of children at a mean follow up of 28 months after minimally invasive GT still required jejunal feeding and Gallo et al found 33% needed jejunal feeding up to a median of 14 years of age [22]. Our data suggests jejunostomy use might decrease into adulthood.

Dumping syndrome is well-recognised after GT and may contribute to poor nutrition. Spitz previously reported an incidence of 4% on reviewing 192 GTs (including the patients in this cohort) [25]. We found in adulthood 4 (12%) participants had a formal diagnosis of dumping syndrome whilst 8 (25%) reported dumping symptoms without a diagnosis and in 4 participants without an understanding of the condition and its association to GT. Dingemann et al [14] found higher
numbers of patients reporting dumping symptoms in adulthood (52%) suggesting this has been previously under reported. All but one of the participants interviewed managed their dumping symptoms by simply eating smaller meals more often, usually with good effect.

The reported need for early reoperation after oesophageal replacement, and incidence of strictures have been used as a comparator between GT and other types of oesophageal replacement. [4-6] However, the longer term need for surgical intervention is poorly reported. We found 3 participants required major revision surgery after leaving paediatric care. Two cases were reportedly performed to overcome poor gastric emptying. Anastomotic dilatation in adulthood was necessary in 11/32 (34%) of GT participants compared with 13% of the PR participants. Meta-analysis suggest that strictures occur in 22% of children undergoing GT [20]. 72% of our participants who needed dilatation as adults had required dilatation as children and secondary GT participants were more likely to need dilatations probably reflecting their more complex surgical course.

In those participants (13/32) who had undergone gastroscopy in adulthood, one reported a diagnosis of Barrett’s oesophagus in the proximal oesophageal remnant. Barrett’s oesophagus is well reported following primary OA repair [10] and also interestingly in the proximal oesophageal remnant of patients previously treated with GT for achalasia in the adult population [28]. Although we recognise the limitations of drawing conclusions from one patient this is an important finding given concern raised in other studies about the fate of the proximal native oesophagus after GT [28]. The incidence of Barrett’s changes may be higher but data is limited to participant recall rather than from clinical notes. As transition care models are being developed for oesophageal atresia, including surveillance endoscopy, it is important that the possibility of Barrett’s oesophagus, metaplasia and subsequent malignancy may occur in the remaining oesophagus following GT is an issue that is considered and conveyed to the adult care team.

There is no doubt that upper gastrointestinal symptoms continue into adulthood in OA patients [10, 11, 13, 29] and we have demonstrated this in both the GT and PR groups. After GT the predominant reported symptom was gastro-oesophageal reflux (60% of participants reporting weekly symptoms). PR participants also frequently reported reflux but only 40% on a weekly basis. However, half of PR participants report dysphagia versus 38% of GT participants. Both GT and PR participants reported a higher GSRS reflux score and indigestion score than that reported for the normal population [17]. Spitz recognised early swallowing problems being universal after GT and severe in around 30% of patients [25] and our latest data suggests a similar number of patients have regular dysphagia in adulthood.

Anaemia remains a long-term problem after GT, reported in nearly half of GT participants and only 3(9%) of the PR group. Most were unaware of the type of anaemia they suffered from. Anaemia after GT is reported in 30% [23], 70% [24] and 100% [20] of children having GT and low ferritin is described [23]. Most authors suggest poor iron absorption is the primary cause with some also suffering UGI bleeding as we experienced. Whilst we recognise the limitations of patient reported anaemia in our study the apparent prevalence compared to the PR group and reports in other studies suggest following GT consideration should be made for long term screening for anaemia and iron deficiency.

Chronic respiratory disease in OA[10, 30] is well reported and may be the result of problems such as tracheomalacia and reflux. After GT the presence of the stomach in the chest can also bring additional problems and decreased functional lung capacity[23, 24]. A quarter of our participants reported chronic respiratory disease and described a range of severity from mild reactive airway disease to severe lung disease and bronchiectasis necessitating care by respiratory physicians. This
aspect of GT follow up receives little attention from surgeons but the frequency and importantly severity in some cases that we report make clear the importance of good early respiratory care and follow-up in these patients.

Spitz, using a modified GIQLI, reported near-normal quality of life in those who had GT as the primary surgery for repair of long gap OA versus those having GT as a salvage procedure who had significantly lower scores and health related QoL[31]. More recently Dingemann et al, reported health related QoL in complex OA, comparing delayed primary anastomosis, patients needing multiple dilations, those who had major revision surgery and oesophageal replacements[14]. They suggest that children have an excellent HRQoL after complex OA repair, including after oesophageal replacement, in comparison with normal controls. However, adults with complex OA demonstrated reduced quality of life with high incidence of reflux, dysphagia and dumping syndrome. We found similar reduced HRQoL in adult GT participants compared to the normal population but also found nearly a quarter of GT participants report higher HRQoL than the normal population. There was no statistical difference in HRQoL compared to PR participants which may be a result of the relatively small sample and significant comorbidities in several PR participants.

The decreased HRQoL and high incidence of adulthood morbidity may help explain the high incidence of diagnosed depression in our study (19% in GT participants). Dingemann et al[14] reported that a similar proportion of adults with complex OA reported QoL scores that would put them at risk of depression but did not provide data on clinically diagnosed depression. Aetiology in depressive illness is multifactorial and interviews in this study provided subjective evidence that in some participants complications from GT, such as self dilating recalcitrant strictures effected QoL as did significant comorbidities such as a participant with renal failure having undergone two renal transplants. These results highlight the need for attention to be paid to this groups risk of mental illness irrespective of causation.

Whilst this study gives the most detailed and long term follow up in adulthood of gastric transposition in OA to date, it has limitations. The total number of participants remains relatively small due to the rarity of the condition making data analysis more difficult. A larger cohort could have been obtained by including overseas patients treated during this period but methodologically, ethically, and practically these patients would have been difficult to contact and interview. This also introduces some degree of selection bias to the cohort investigated. We also recognise that those with good outcomes may be more willing to participate in such studies than those with poorer outcomes although anecdotally that did not appear to be the case. In comparison to previous work the numbers of participants was good and given the historical nature of the cohort the response rate was excellent. Larger multi-centre studies would address this issue and allow multi variate type analysis to identify risk factors for poorer outcomes and QoL.

We recognise that the QoL tools we have used are not directly validated for use in the OA population which may be a reason we found little statistical difference between groups. However the use of these tools in the literature for allied conditions such as gastroesophageal reflux and in other OA studies we feel gives some informal validation to their use in this study. Our use of telephone interviewing as opposed to written questions may bias responses including in the validated questionnaires but did positively influence recruitment and gave the chance to gain a wider qualitative understanding of this patient group. Patient reported outcomes limit accuracy of data however the impracticality and ethics involved in accessing current adult medical records meant obtaining more accurate data was not possible. One other inevitable consequence of long-term follow up studies is that the data reflect surgical and medical practise initiated historically and results obtained may not reflect current practise. We recognise the lack of endoscopic follow up in
this study and this is the result of a reliance of patients reported outcomes and the historic nature of the study when neither managed transitional care or endoscopic surveillance were routine.

Although there are clearly alternative surgical options for these patients, we currently do not have similar comprehensive long term outcome data of these alternatives in adulthood as comparison. Such comparison was therefore not the purpose of this study. We recognise there is no perfect oesophageal substitute and the limited data available suggest that patients who have other forms of oesophageal replacement are also likely to suffer from significant morbidity into adulthood. The morbidity seen in the long term from complex oesophageal atresia must be a reflection of the combination of complexity of the condition, its treatment and associated anomalies as opposed to simply the surgical techniques used to correct it.

Conclusions

We have demonstrated the most detailed long term follow up in adulthood of gastric transposition for OA to date and report the broad spectrum of outcomes experienced by these patients. From those with multiple significant morbidities, daily symptoms and low quality of life to over a quarter who have a normal health related quality of life, several of who report living a ‘normal life’ and working in a variety of full time professions. The frequency of significant surgical and medical problems across the cohort and associated detriment on mental health mandates long term follow up of all patients undergoing gastric transposition for OA into adulthood and quality transition of care from paediatric to adult services. This transition needs to be of high quality, multi-disciplinary in nature and may involve many teams including surgeons, gastroenterologists, respiratory physicians, general practitioners and mental health teams.

Acknowledgments

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This study was not preregistered with an independent institutional registry.

Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to the corresponding author.
### Tables

<table>
<thead>
<tr>
<th></th>
<th>Gastric Transposition (GT) n = 32</th>
<th>Primary Repair (PR) n = 32</th>
<th>P value</th>
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<tbody>
<tr>
<td><strong>Childhood Demographics</strong></td>
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<tr>
<td>Gender</td>
<td>50% Male</td>
<td>56% male</td>
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</tr>
<tr>
<td>Type of OA</td>
<td>Type A = 40%, Type C = 47%, Type B = 3%, Type D = 10%</td>
<td>Type A = 3%, Type C = 94%, Type D = 3%</td>
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<tr>
<td>Associated abnormalities</td>
<td>21 (66%)</td>
<td>19 (60%)</td>
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<tr>
<td>Vertebral</td>
<td>5 (16%)</td>
<td>4 (13%)</td>
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<tr>
<td>Anorectal</td>
<td>8 (25%)</td>
<td>7 (22%)</td>
<td></td>
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<tr>
<td>Cardiac</td>
<td>9 (28%)</td>
<td>7 (22%)</td>
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<tr>
<td>Renal</td>
<td>10 (32%)</td>
<td>4 (13%)</td>
<td></td>
</tr>
<tr>
<td>Limb</td>
<td>3 (9%)</td>
<td>2 (6%)</td>
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<tr>
<td>Duodenal atresia</td>
<td>3 (9%)</td>
<td>0 (0%)</td>
<td></td>
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<tr>
<td>Other</td>
<td>3 (9%)</td>
<td>2 (6%)</td>
<td></td>
</tr>
<tr>
<td>Primary vs Secondary</td>
<td>56% Primary vs 44% Secondary</td>
<td></td>
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<tr>
<td><strong>Adulthood Demographics</strong></td>
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</tr>
<tr>
<td>Mean age (SD) years</td>
<td>29 ± 5</td>
<td>29 ± 5</td>
<td></td>
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<tr>
<td>Mean BMI (SD)</td>
<td>19.9 ± 3.5</td>
<td>24.2 ± 4.9</td>
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<tr>
<td>In relationship (married / partner)</td>
<td>10 (31%)</td>
<td>18 (56%)</td>
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<tr>
<td>Employed</td>
<td>26 (81%)</td>
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<tr>
<td>Full time</td>
<td>20</td>
<td>25</td>
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<td>Part time</td>
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Table 1. Demographics

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<th>Primary Repair (PR) n = 32</th>
<th>P value</th>
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<tbody>
<tr>
<td><strong>Morbidity</strong></td>
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<tr>
<td>Supplementary feeding</td>
<td>6 (19%)</td>
<td>0 (0%)</td>
<td>0.02</td>
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<tr>
<td>Dumping symptoms</td>
<td>8 (25%)</td>
<td>0 (0%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Major revision surgery</td>
<td>3 (9%)</td>
<td>0 (0%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Anastomotic dilatation</td>
<td>11 (34%)</td>
<td>4 (13%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Chronic respiratory disease</td>
<td>9 (28%)</td>
<td>8 (25%)</td>
<td>0.9</td>
</tr>
<tr>
<td>Severe respiratory disease</td>
<td>3 (9%)</td>
<td>0 (0%)</td>
<td>0.2</td>
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<tr>
<td>Anaemia</td>
<td>15 (47%)</td>
<td>3 (9%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Ulcers / upper GI bleeding</td>
<td>3 (9%)</td>
<td>0 (0%)</td>
<td>0.2</td>
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<tr>
<td>Depression</td>
<td>6 (19%)</td>
<td>3 (9%)</td>
<td>0.4</td>
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<td><strong>Medication</strong></td>
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<tr>
<td>Anti-reflux</td>
<td>11 (34%)</td>
<td>8 (25%)</td>
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<td>Inhalers</td>
<td>9 (27%)</td>
<td>7 (22%)</td>
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Table 2. Adulthood morbidity and medication

Legends:

Figure 1. Recruitment flow chart
Figure 2. Frequency of symptoms
Figure 3. GSRS Total scores
Figure 4. GSRS Sub-scale scores
Figure 5. GIQLI scores by group
Figure 1

GT for OA n = 117

- Excluded Non UK based n = 61
- No address n = 4
- No telephone reply n = 8

- Invitations sent n = 44

- Declined n = 12

- Completed interview n = 32

- Validated questionnaires n = 30
- Interview only via proxy n = 2
Figure 2
Figure 3
Figure 4
Figure 5

- **GIQLI by Group**

  - Normal Population
    - Mean (SD)

  - GIQLI Score
    - 130
    - 120
    - 110
    - 100
    - 90

- GT
- PR

  - $p = 0.29$