Management of perforated duodenal peptic ulcer treated by suture

Prise en charge de l'ulcère peptique duodénal perforé traité par suture

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RÉSUMÉ

Introduction : La chirurgie laparoscopique est devenue le gold standard pour de nombreuses interventions en raison de ses avantages, comme un séjour post opératoire plus court, une reprise de l'activité plus rapide et moins de douleurs postopératoires. Cependant, le choix de l'approche laparoscopique d'un ulcère peptique duodénal perforé reste toujours débattu en raison de l'absence de bénéfices significatifs.
Le but de notre travail est d'évaluer la prise en charge de l'ulcère peptique duodénal perforé traité par suture.
Méthodes: Il s'agit d'une étude rétrospective colligeant 81 patients opérés pour ulcère duodénal perforé entre le 1er Juin 2012 et le 31 Décembre 2016 qui ont été opéré au service de chirurgie B de l'hôpital Charles Nicolle.
Résultats: Notre étude rétrospective a montré que l'approche laparoscopique avait une durée de séjour post opératoire plus courte (3 [1-5] contre 4 [1-16] jours, p< 0,001), un taux de mortalité plus bas (3% contre 19%, p = 0,032) et plus de suites post-opératoires simples (97% contre 74%, p = 0,004) par rapport à la laparotomie. Les patients qui n'étaient pas admis à l'unité de soins intensifs pendant les 48 premières heures avaient 9,901 plus de chance d'avoir recours à la voie laparoscopique. Les patients qui ont été opérés par des seniors avaient 3,240 fois plus de chance d'être traité par voie laparoscopique. Il n'y avait pas de variable prédictive de conversion. Le taux de mortalité était de 11%. L'âge représentait le seul facteur indépendant prédictif de mortalité avec un cut-off point de 47 ans.
Conclusions: La voie laparoscopique est couramment pratiquée dans l'ulcère duodénal perforé. Dans notre étude, nous avons prouvé que la laparoscopie a permis d'avoir moins de complications post-opératoires, un taux de mortalité plus faible et une durée post-opératoire plus courte par rapport à la laparotomie. La principale limitation de notre étude était la non randomisation et le manque d'expertise en laparoscopie. La décision de pratiquer une laparoscopie ou une laparotomie dépendait de la disponibilité des chirurgiens seniors.

Mots-clés
Ulcère peptique perforé, laparoscopie, sutures, roc curve, logistic regression.

SUMMARY

Background: Laparoscopic surgery has become the gold standard for many procedures owing to its advantages such as a shorter post-operative stay, a faster recovery and less postoperative pain. However, choosing laparoscopic approach in an emergency situation such as in the management of a perforated duodenal peptic ulcer is still debated because of the absence of significant benefits. This study aimed to assess the management of perforated duodenal peptic ulcer treated by suture.
Methods: It's a retrospective study enrolling 81 patients operated on for duodenal perforated peptic ulcer between June 1st, 2012 and December 31st, 2016 who underwent surgery in the surgical department B of Charles Nicolle's Hospital.
Results: Our retrospective study showed that laparoscopic approach had shorter post-operative duration (3 [1-5] versus 4 [1-16] days, respectively, p< 0.001), shorter mortality rate (3% versus 19%, p=0.032) and more uneventful post-operative course (97% versus 74%, p=0.004) comparing to the open approach. Patients who were not admitted in the intensive care unit during the first 48 hours had 9.901 more chance to be operated by laparoscopic approach. Patients who were operated on by a senior had 3.240 times more chance to be operated by laparoscopic approach. There was no predictive variable for conversion. Mortality rate was 11%. Age was the only predictive independent factor of mortality with a cut-off point of 47 years.
Conclusions: Laparoscopic approach is routinely practised in the perforated duodenal ulcer. In our study, we showed that laparoscopic approach had less post-operative complications, a lower rate of mortality and a shorter post-operative duration comparing to the open approach. The main limitation of our study was non-randomization and lack of laparoscopic expertise. The decision for either open or laparoscopic approach was then dependent on senior surgeon's availability.

Key-words
Peptic ulcer perforation, laparoscopy, sutures, courbe roc, régression logistique.

Reports on the laparoscopic procedure for perforated peptic ulcer were first published in 1990 (1). The management of perforated duodenal peptic ulcer has evolved in the past three decades owing to the discovery of the Helicobacter pylori's role in the genesis of the duodenal peptic ulcer, the advent of proton pump inhibitors and antibiotics. Laparoscopic approach was considered as safe as open approach because of a shorter hospital stay, a faster recovery and a less postoperative pain (2).
Laparoscopic surgery has become the gold standard for many procedures such as cholecystectomy. However, choosing laparoscopic approach in an emergency situation such as in the management of a perforated duodenal peptic ulcer is still debated because of the absence of significant benefits (3).
This retrospective study, using an administrative database, aimed to assess the management of perforated duodenal peptic ulcer treated by suture.

METHODS

It's a retrospective study enrolling patients operated on for duodenal perforated peptic ulcer between June 1st, 2012 and December 31st, 2016 who underwent surgery in the surgical department B of Charles Nicolle's Hospital.

ELIGIBILITY CRITERIA:

We included 81 patients aged 19 years old and above, independently of the gender, who were operated on for a perforated duodenal peptic ulcer and underwent laparoscopic or open approach in the surgical department B of Charles Nicolle's hospital.

NON ELIGIBILITY CRITERIA:

We did not include neither the patients who had gastric perforation or hemorrhagic ulcer, nor the patients who had a different procedure than suture of the duodenal ulcer perforation.

SURGICAL APPROACH:

Laparoscopic approach:
The standardized technique of laparoscopic approach for perforated duodenal peptic ulcer consisted in placing the patient in supine position and establishing a pneumoperitoneum up to a pressure of 12 mmHg. The laparoscope was introduced through an 11mm-diameter trocar. After identification of the perforation site, two additional 5mm and 10mm trocars were inserted into the right and left upper quadrants of the abdomen. The sutures were performed intra corporeally by interrupted 2/0 polyglactine. All the compartments of the peritoneal cavity were irrigated with normal saline in variable positions (4). A subhepatic Redon drain was left to surgeon's discretion.

Open approach:
Open approach was usually performed to the patients who were hemodynamically unstable, patients who had anesthetic contraindications for pneumoperitoneum such as cardiorespiratory diseases, and patients who had undergone previous open upper abdominal surgery. Open approach was also used by surgeons who didn't have enough expertise for laparoscopic approach.
The open repair was performed through an upper midline incision. We identified the perforation area. The suturing was performed intra corporeally by interrupted 2/0 polyglactine sutures. An extensive peritoneal toilet was established. Closure of fascia was performed using 1/0 suture (5).

CULLED VARIABLES:

Were culled the following variables: age, gender, comorbidities, previous surgery, admission in an intensive care unit in the first 48 hours, laparoscopic approach, operator (senior/resident), operative time, conversion to open approach, surgical complications, medical complications, respiratory ventilation, mortality, post-operative stay and hospital stay durations.

OUTCOME MEASURES:

The main outcome measure was: Post-operative mortality defined as death that occurred during the hospital stay or within 30 days after surgery (4).
The other secondary outcome measures were:
1/ Operative time
2/ Conversion to open approach
3/ Post-operative complications defined as complications that occurred during the hospital stay, which may be related to the comorbidities or to the performed surgery. The types of complications analyzed were: medical complications, surgical complications with re-intervention, suture leakage, intra-abdominal collection and mortality. A surgical site infection (SSI) was defined as infection occurring within the 30 days after intervention (4).
4/ Post-operative hospital stay

STATISTICAL ANALYSIS:

Data were analyzed with SPSS software (Statistical Package for the Social Science, SPSS, Inc; version 23.0). Bivariate analysis was performed on all factors with the chi-square test and Fisher's exact test for qualitative variables and the Student's t-test for quantitative variables. When the distribution was not Gaussian, the Mann-Whitney U test was used. All variables with a p value ≤ 0.05 were introduced into a logistic regression model. For continuous variables retained as predictive, we applied receiving operating characteristic (ROC) curve to identify the cut-off point with the best couple sensitivity and specificity. We calculated the area under the curve with its $^{95\%}$CI.

RESULTS

Descriptive analysis:

Seventy men (86%) and 11 women (14%) were included according to eligibility criteria. The mean age (± standard) was 44.7±18.57 years. Laparoscopic approach (LA) was performed for 38 patients (47%) and open approach (OA) for 43 patients (53%). Laparoscopic approach was performed by a resident for 47 patients (58%) and by a senior for 34 patients (42%). Six patients (16%) underwent conversion to open approach. The median operative time [range] was 1h30 [0.45- 3.30]. Twelve patients (15%) had post-operative complications such as suture leakage reported in two patients (33%) and one case (17%) of intra-abdominal collection. Mortality rate was 11% (Table 1).

Table 1: Baseline characteristics of patients: Univariate analysis (n= 81)

Variables	N (%) or median (range)
Demographics	
Mean Age ±SD (years)	44.70±18.57
Gender, male	70 (86%)
Comorbidities	21 (26%)
Previous surgery	12 (15%)
Admission in an ICU* during the first 48 hours	14 (17%)
Organ system failure	4 (5%)
Operation variables	
Laparoscopic approach	38 (47%)
Operator (resident)	47 (58%)
Median Operative time [Range] (hours)	1.30 [0.45- 3.30]
Conversion	6 (16%)
Post-operative course	
Uneventful	69 (85%)
Surgical complications with re-intervention	6 (7%)
Suture leakage	2 (33%)
Intra-abdominal collection	1 (17%)
Medical complications	13 (16%)
Respiratory assistance (days)	5 [1-9]
Mortality	9 (11%)
Post-operative stay (median [ ] IQR [ ])	4 [1,16] IQR** [3,5]
Hospital stay duration (median [ ] IQR [ ])	4 [1,16] IQR** [3,5]

ICU*: Intensive care unit, IQR**= Interquartile range

Laparoscopic approach versus open approach:

Twelve patients (28%), who were admitted in an intensive care unit (ICU) during the first 48 hours, underwent an OA versus two patients (5%) who underwent a LA. The median operative time for LA versus OA did not differ statistically 1h45 [0.45-3.20] versus 1h30 [0.50-3.30], respectively (p = 0.301). Post-operative course was uneventful for 37 (97%) patients in LA comparing to 32 patients (74%) in the OA with a statistical significative difference (p=0.004). Mortality rate in LA was inferior to OA (3% versus 19%, p=0.032). Median duration of post-operative stay for the LA was shorter than the median duration of the OA (3 [1-5] versus 4 [1-16] days, respectively, p< 0.001) (Table 2).

Table 2: Laparoscopic versus open approach: Bivariate analysis (n= 81)

Variables	Laparoscopic group (n=38)	Open group (n=43)	p
Demographics			
Mean Age ±SD (years)	42.05±15.56	47.05±20.78	0.424
Gender, male	34 (90%)	36 (84%)	0.451
Comorbidities	6 (16%)	15 (35%)	0.050
Previous surgery	6 (16%)	6 (14%)	0.816
Admission in an ICU during the first 48 hours	2 (5%)	12 (28%)	0.007
Operation variable			
Median Operative time [Range] (hours)	1.45 [0.45-3.20]	1.30 [0.50-3.30]	0.301
Operator (resident)	18 (47%)	29 (67%)	0.068
Post-operative course			
Uneventful	37 (97%)	32 (74%)	0.004
Surgical complications with re-intervention	0 (0%)	6 (14%)	0.027
Medical complications	1 (3%)	12 (28%)	0.002
Mortality	1 (3%)	8 (19%)	0.032
Post-operative stay (days)	3 [1-5]	4 [1-16]	<0.001
Hospital stay duration (days)	3 [2-5]	4 [1-16]	0.002

Logistic regression was performed to identify variables explaining the surgeon's tendency to choose laparoscopic approach. Senior operator preferred LA than OA (senior/resident) (OR= 3.240, $^{95\%}$CI [1.185 8.857], p= 0.022). The patients who were not admitted in the ICU during the first 48 hours had more chance to have a laparoscopic approach (OR $^{(\text{No admission/Admission})}$ = 9.901, $^{95\%}$CI [1.892 51.801], p= 0.007).

Conversion versus no conversion:

The median operative time was longer in the conversion group 2h02 [1.20-3.20] than in the 'no conversion' group 1h35 [0.45-3.00] but it did not reach the level of significance (p=0.068). Post-operative course was uneventful for 32 patients (100%) who didn't have conversion from laparoscopy to open approach versus five patients (83%) who had conversion, without a statistically significant difference p= 0.158 (Table 3).

Mortality factors:

Of 81 patients, nine died during post-operative course. Three were classified in grade 1 of the American Society of Anaesthesiologists (ASA). Four patients were classified grade 2 and two patients were classified grade 3 of ASA.

Two ASA 1, one ASA 2 and one ASA 3 had multiple organ system failure in admission.

Table 3: Conversion versus no conversion: Bivariate analysis (n= 38)

Variables	Laparoscopic conversion (n=6)	No conversion (n=32)	p
Demographics			
Mean Age ±SD (years)	46.33±22.08	41.25±14.35	0.861
Gender, male	6 (100%)	28 (88%)	1.000
Comorbidities	1 (17%)	5 (16%)	1.000
Previous surgery	2 (33%)	4 (12%)	0.234
Admission in an ICU during the first 48 hours	1 (17%)	1 (3%)	0.294
Operation variables			
Median Operative time [Range] (hours)	2.02 [1.20-3.20]	1.35 [0.45-3.00]	0.068
Operator (resident)	3 (50%)	15 (47%)	1.000
Post-operative course			
Uneventful	5 (83%)	32 (100%)	0.158
Medical complications	1 (17%)	0 (0%)	0.158
Mortality	1 (17%)	0 (0%)	0.158
Post-operative stay (days)	3 [1-4]	3 [2-5]	0.126
Hospital stay duration (days)	3.5 [2-4]	3 [2-5]	0.598

A bivariate analysis allowed us to identify predictive factors of mortality (Table 4). These mortality factors were age (p=0.002), comorbidities (p=0.046), hospitalisation in an ICU during the first 48 hours (p<0.001), longer operative time (p=0.018), open approach (p=0.032), surgical complications with re-intervention (p<0.001) and medical complications (p<0.001) (Table 4).

Logistic regression identified "age" as the only independent variable associated to mortality (OR=1.053, $^{95\%}$CI [1.014 1.093], p=0.007) with an Area Under the Curve AUC= 0.813 $^{95\%}$CI [0.701 0.924], p=0.002 (Figure 1). The probability of death increased with age (e.g. Mortality rate was 48.3% when patients were 90 years old) (Table 5).

The informative indices of the cut-off point of 47 years old were: Sensitivity (89% 95%CI [68 100]), Specificity (69% 95%CI [59 80]), Positive predictive value (27% [11 42]), Negative predictive value (98% [94 100]), Positive Likelihood ratio (2.91 [1.92 4.42]) and Negative Likelihood ratio (0.16 [0.03 1.02]). On other words, the cut-off point 47 years old had good sensitivity and negative predictive value.

Table 4: Predictive factors of mortality: Bivariate analysis (n= 81)

Variables	Deceased (n=14)	Alive (n=67)	p
Demographics			
Mean Age ±SD (years)	62±15.86	42.54±17.82	0.002
Sex, male	6 (67%)	64 (89%)	0.100
Comorbidities	16 (22%)	5 (56%)	0.046
Previous surgery	3 (33%)	9 (12%)	0.125
Hospitalization in an ICU during the first 48 hours	9 (100%)	5 (7%)	<0.001
Operation variables			
Median Operative time [Range] (hours)	2.10 [1.20-2.30]	1.30 [0.45-3.30]	0.018
Operator (resident)	4 (44%)	43 (60%)	0.481
Conversion	1 (100%)	5 (13%)	0.158
Open approach	1 (11%)	37 (51%)	0.032
Post-operative course			
Surgical complications with re-intervention	5 (6%)	1 (1%)	<0.001
Medical complications	9 (100%)	4 (6%)	<0.001
Post-operative stay (days)	4 [1-9]	4 [1-16]	0.764
Hospital stay duration (days)	4 [1-9]	4 [2-16]	0.643

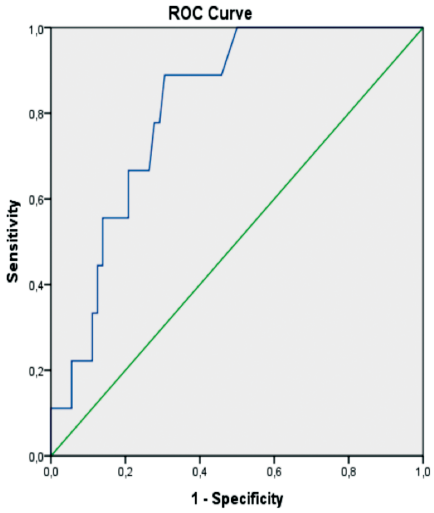

Figure 1: ROC curve: age
Area Under the Curve AUC= 0.813 95%CI [0.701 0.924], p=0.002

Table 5: Probability (p) of Death/Age

Age (years)	P
50	10.4%
60	16.4%
70	24.8%
80	35.7%
90	48.3%

DISCUSSION

This retrospective study showed that LA had shorter duration of hospital stay (3 [2-5] versus 4 [1-16] days, respectively, p= 0.002), shorter mortality rate (3% versus 19%, p=0.032) and more uneventful post-operative course (97% versus 74%, p=0.004) comparing to the OA. Patients who were not admitted in the ICU during the first 48 hours had 9.901 more chance to be operated by LA and patients who were operated by a senior had 3.240 times more chance to be operated by LA. There was no predictive variable for conversion. Mortality rate was 11% and age was the only predictive independent factor of mortality with a cut-off point of 47 years.

There was a statistical difference in favour of LA to suture perforated duodenal peptic ulcer regarding comorbidities (p=0.050) and admission in an ICU in the first 48 hours (p=0.007). As concerns the outcome measures, there was less surgical complications with re-intervention (p=0.027), less medical complications (p=0.002), less mortality rate (p=0.032) and a shorter post-operative stay (p<0.001) for the LA.

This study was based on variables culled from administrative data which are defined as 'large computerized data files generally compiled in billing for health care services such as hospitalizations (6). As stated by Guller, surgical outcomes research based on administrative data should be viewed as being complementary and not inferior to randomized clinical trial. Comparing to randomized clinical trials, administrative data are less expensive and time consuming (7). Moreover, administrative database permits the performance of descriptive analyses and the comparison of two surgical methods over a longer study period (8). It allows researchers to answer questions that can't be answered through a randomized clinical trial because of its complexity, its high price and some ethical problems (9).

Our study included 81 patients with a mean age of 44.7±18.57 years with a majority of men (86%). These results were consistent with the results of Bertleff & Lange (10) and Vaidya (11) who reported in their studies a mean age of 48 years and 38.5 years respectively, with a male predominance.

Only 21 (26%) patients in our study had associated comorbidities: Arterial hypertension (4 patients), diabetes (2 patients) and respiratory disease (2 patients). These data were matched with Abdelaziem (32%) (12) and Hung-Chieh (35%) (13) studies.

The median operative time was 1h30 [0.45- 3.30] which was consistent with Bertleff & Lange (10) Linevicius and Morkevicius (14) and Lam (15) who reported an operative time of 75, 76.2 and 86 minutes, respectively.

The duration of post-operative stay for the LA group was shorter than those of the OA group 3 [1-5] versus 4 [1-16] days (p<0.001). Bujun (17) reported the same results 7 [5–9] versus 8 [7–10] days (p < 0.001).

Six patients (16%) underwent laparoscopic conversion to midline approach among which two conversions were due to a dissection difficulties by LA. This rate was in accordance with many other studies like Bertleff & Lange (10) and Vaidya (11) who reported conversion in four patients out of 52 (8%) and two patients out of 31 (6.5%) respectively.

Twelve patients (15%) had post-operative complications: Two patients had suture leakage (33%) and one patient had intra-abdominal collection (17%). Lunevicius (14) reported four cases with suture leakage. Bertleff (10) and Abdelaziem (12) also reported a leakage rate of 3.8% and 4%, respectively. As concerns intra-abdominal collection, Elbroend & Andersen (16) reported that 10% had intra-abdominal abscess.

Post-operative course was uneventful for 37 (97%) patients in laparoscopic group comparing to 32 patients (74%) in the open group with a statistically significant difference (p=0.004). Chunhua's meta-analysis, which included 24 non-randomized controlled studies, demonstrated a lower overall rate of postoperative complications in the LA group (RR= 0.49; $^{95\%}$CI, [0.27 0.88]; p= 0.018) (18).

Mortality rate was recorded in nine patients (11%). LA group had less mortality than OA group (3% versus19%, p=0.03). Logistic regression retained age as an independent variable associated to mortality (OR=1.053, $^{95\%}$CI [1.014 1.093], p=0.007). Linevicius & Morkevicius reported 20 deaths (9%), all in the OA group [14]. Antoniou's meta-analysis (19) reported three deaths in the LA group and eight deaths in the OA group, giving rates of 2% and 6%, respectively (OR= 0.36, $^{95\%}$CI, [0.10 1.32], p=0.124).

In our study, six patients (14%) underwent re-intervention after surgical complications in the OA group versus no re-intervention (0%) for the LA group. However, in Antoniou's meta-analysis (19), one percent of the laparoscopic group and 8% of the open group underwent repeated surgery (OR= 2.02, $^{95\%}$CI, [0.33 12.36], p=0.446).

On the other hand, there were some divergence between our study and other articles of medical literature. Lo (13) and Lee (20) reported an operative time of 50 minutes and 20.7 ± 4.9 minutes, respectively. This operating time can be reduced with laparoscopic expertise such as the use of a powerful washing system to reduce peritoneal toilet's time. Abdelaziem (12) had less post-operative complications as only 4% had developed pelvic intra-abdominal collection. There was no statistically significant difference between LA and OA in terms of hospital stay (5 versus 5.33 days; p= 0.37) in Ates's study (21). No mortality was encountered neither in Abdelaziem (12) nor in Khelifi studies (22).

The main limitation of our study was non-randomization and lack of laparoscopic expertise. The decision for either

open or laparoscopic approach was then dependent on senior surgeon's availability. Furthermore, administrative databases can contain coding errors, lack of clinical data and are not able to answer to specific research questions (23). That's why, they should be carefully interpreted.

CONCLUSIONS

Laparoscopic approach is routinely practised in the perforated duodenal ulcer. In our study, laparoscopic approach had less post-operative complications, a lower rate of mortality and a shorter post-operative duration comparing to the open approach. Besides, we reported that patient's age was the only independent factor which increased mortality rate with a statistically significant difference (OR=1.053, $^{95\%}$CI [1.014 1.093], p=0.007). Moreover, we concluded that the operator (resident/senior) (OR= 3.240, $^{95\%}$CI [1.185 8.857], p= 0.022) and the admission in the intensive unit care in the first 48 hours (no admission/ admission) (OR= 9.901, $^{95\%}$CI [1.892 51.801], p= 0.007) were the only variables related to laparoscopic approach.

However, laparoscopic approach needs expertise to reduce the incidence of conversion. We need a randomized prospective study to confirm the advantages of laparoscopic approach.

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