SURGICAL TREATMENT OF ABNORMAL UTERINE BLEEDING (AUB-O,E,N): A COST-EFFECTIVENESS STUDY USING THE FRENCH HOSPITAL CLAIMS DATABASE

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August 3, 2020

Abstract

Objective: AUB-O,E,N is treated first with medical management, followed by surgery, which failure or complications have significant burden. The objective was to perform a cost-effectiveness analysis of four surgical strategies, comparing cost and avoided failure rate, using the French PMSI database. Design: Retrospective analysis performed using the French exhaustive national hospital discharge database (PMSI). Population: All incident 35-55 year-old women operated on for four types of AUB-O,E,N surgery (2nd generation, 1st generation, curettage or hysterectomy) between 2009 and 2014 were included. Methods : They were followed to collect rehospitalizations related to failure or complication and their cost, during at least 18 months. Hospital costs were estimated using the French tariffs in 2017/euro. Main Outcome measures : A cost-effectiveness analysis was performed comparing each surgical procedure to 2G, in hospitalization costs and rate of patients without failure. Results : The study included 88,154 patients. At 18 months, mean cost per patient was \euro2,448 for 2G, \euro2,100 for 1G, \euro2,275 for curettage and \euro4,157 for hysterectomy. Hysterectomy was the most effective strategy in terms of absence of failure, but also the most expensive, with an incremental cost of \euro24,008 per additional % of patient without failure. Even with a mean cost similar to 2G, curettage was the least effective strategy with a failure rate reaching 20.6% at 18 months. 1G was less expensive but also less effective than 2G, with an economy of \euro13,078 per % of patient without failure loss. Conclusion: 1G and 2G techniques are the most efficient strategie

Introduction

Heavy menstrual bleeding is defined as excessive menstrual blood loss of 80 mL per cycle, for more than 7 days which interferes with a woman's physical, social, emotional and/or quality of life^{1,2} and affects approximately 10%-30% of all women worldwide once in their lifetime^{3,4}. FIGO defined a new terminology for normal and abnormal uterine bleeding (AUB) in the reproductive years and for classification cases with PALM-COEIN⁵. The causes of dysfunctional uterine bleeding are now defined by O,E,N (Ovulatory dysfunctional, Endometrial, Not otherwise classified). The causes defined by C (Coagulopathology) and I (Iatrogenic)

have no indication for surgical treatment. Medical treatment is usually the first intent treatment. Except for curettage, surgical interventions are recommended for women with severe AUB-O,E,N who do not wish to become pregnant^{6,7}. In this case, different surgical interventions are routinely performed for treatment, the choices include second-generation (2G) endometrial ablation techniques (thermal balloon, microwave, cryoablation, radiofrequency) and first-generation (1G) techniques (endometrectomy, roller-ball and laser ablation), whereas a first-line curettage or hysterectomy is no longer recommended in France⁷. Hysterectomy is effective but has more complications than endometrial ablation; endometrial ablation techniques are less invasive but could ultimately lead to hysterectomy in 20% of cases within 5 years ⁸. 2G procedures seem to be as effective as 1G procedures and present with fewer complications, like operating time decrease, and can be used more often with local anesthesia ⁹⁻¹¹. In 2019, the HEALTH randomized controlled trial ¹² compared laparoscopic supracervical hysterectomy *versus* endometrial ablation (2G or 1G) for surgical treatment of heavy menstrual bleeding for 660 patients. Hysterectomy showed to be superior in terms of clinical effectiveness, with similar rate of complications but takes longer time in operating room, a longer hospital stay and longer recovery time, then increasing the cost of the radical procedure.

Regarding the economic evidence of surgical procedures, a French retrospective study showed that hysterectomy was the most effective but also the most expensive strategy in 2003, as compared to 2G techniques¹³. The recent economic analysis of the HEALTH trial in UK confirmed that hysterectomy expenses is higher of £1604 at 15 months¹⁴. Two trial-based cost-utility analyses demonstrated that 2G endometrial ablation were more cost-effective than 1G devices^{15,16}, but their external validities was questionable regarding limitations in available data to build the model. In real conditions, an economic analysis based on the German health claims database showed that a 2G technique (radiofrequency ablation) was associated with fewer recurrences, lower rates of subsequent surgical treatments and lower costs than other ablation techniques¹⁷. The replicability of this study was however questionable, as it only concerned 88 patients. The most complete economic study was done by Miller *et al* in 2015 in the US context¹⁸, who performed a semi-Markov model at 1, 3 and 5-years using the data of 63,482 patients from three large medical claims databases in real-conditions to compare Novasure*versus* other ablation modalities and hysterectomy. To date, there is no similar cost-effectiveness analysis comparing surgical strategies of AUB, that used only data from a hospital claim database, reflecting real-life practice in the European context.

Since the introduction of a DRG-based prospective payment system in France in 2005, the PMSI-MCO database has been used as the basis for the funding of services in all hospitals. Indeed, its high exhaustiveness and the quality of its information allow using this database for epidemiologic, burden of disease, or economic analyses in real-life conditions. As individual patients can be tracked across multiple hospitalizations over time through a unique anonymous patient identifier (with the patient's social security number, date of birth and gender) which is kept unchanged until the patient dies, a patient can be followed-up during many years. Several years after the implementation of recommendations for the management of menorrhagia in France⁷, there is a need to compare the different surgical techniques in real life conditions, by comparing both their respective efficacy (expressed in terms of the absence of failure and/or complication) and their associated hospitalizations costs along time. In the present study, the French PMSI-MCO database was used to perform a cost-effectiveness analysis, comparing 2G endometrial ablative techniques to 1G techniques, curettage and hysterectomy for treating AUB-O,E,N.

Methods

Data sources

Data were retrospectively extracted from the French Hospital Medical Information database (Programme de Médicalisation des Systèmes d'Information – PMSI). The French PMSI-MCO database covers all overnight or day hospitalizations in the public and private French hospitals¹⁹. Each hospital stay results in a production of a standard discharge summary ("Résumé de Sortie Standardisé" RSS) following inpatient conventional stays, day-hospital stays or sessions. The RSS is then anonymized to become the RSA ("Résumé de Sortie Anonyme"). The RSA contains information's on the patient characteristics (gender, age, residence code), on the main diagnosis that led to hospital admission, on the nature of the treatment and work-up (examinations) carried out, on comorbidities and on complications. Diagnoses are coded using the International Classification of Diseases, 10th revision (ICD-10)²⁰ either as primary- (PD: the condition for which the patient was hospitalized), related- (RD: any underlying condition which may have been related to the PD), or significant associated-diagnoses (SAD: comorbidities or complications which may affect the course or cost of hospitalization). For each DRG produced, the hospital receives a payment which amount corresponds to the national tariff of DRG, intending to cover all hospital expenses.

Since a patient may have several hospital stays during a year, it is possible to count the number of stays or the total cost of hospitalization per year, by linking all his hospital stays based on his patient's identification number.

Identification of patients operated on for menorrhagia

The first step consisted in identifying within the PMSI-MCO database all the hospitalizations of 35-55 year-old women who had a first surgical management of menorrhagia in France from 1st January 2009 until 30th June 2014. Detailed information's regarding the algorithm used has already been described²¹. Briefly, stays for surgical treatment (with a CCAM code figuring in the Sup. Table 1) as PD or RD in patients with menorrhagia (with an ICD-10 code figuring in the Sup. Table 2) were selected. Patients already operated on for menorrhagia surgery were excluded, to include incident patients only. Any patient identified as presenting comorbidities, concomitant conditions (breast or colorectal cancer), treatments potentially causes of bleeding (Willebrand disease, myoma respectively, C and L of new terminology⁵), as well as patients with gynecological cancers, alcoholic liver, gynecological and pelvic infections and inflammation, endometriosis, uro-gynaecological prolapse, fistulas, polyps and dysplasia, infertility, pregnancy, spina bifida, iatrogenic causes (I of new terminology⁵) or blood diseases were excluded as they would introduce bias.

Stays were classified into one of four categories of surgical techniques to treat AUB-O,E,N according to the CCAM code (Online supporting material 1): (i) second-generation (2G) endometrial ablation techniques such as radiofrequency ablation or balloon thermodestruction, (ii) first-generation (1G) endometrial ablation and/or resection techniques, such as loop resection and/or roller ball, (iii) curettage and (iv) hysterectomy. Thanks to their unique anonymous identifier, all patients were followed from their initial surgery for at least 18 months and up to date point (31/12/2015) or death, in order to detect any severe complications or failure.

Effectiveness criteria: rate of patients without failure or complication

In this cost-effectiveness analysis, the main criterion used to express the effectiveness of the initial menorrhagia surgery was the rate of patients without failure over time, for each surgical category. Using a *time-to-event* variable allowed considering both the proportion of failures that occurred in each surgical group and their time of occurrence. Failure (considered as the event) was defined as the first re-hospitalization that occurred either as i) stay for new bleeding surgery (Online supporting material 2), ii) stay containing a menorrhagia CIM-10 code stated as main- or related-diagnosis or iii) stay containing any CIM-10 codes for pregnancy.

As a secondary endpoint, effectiveness of the initial AUB surgery was also compared between strategies using the rate of patients without severe complications over time. Severe complication was defined as the first event that occurred either as 1) re-hospitalization during the 30 days following the surgery due to anemia, shock, any complication directly linked to the surgical intervention, pain, infection, blood supply, inflammatory disorders or hemoperitoneum within urologic, genital, abdominal or pelvic location or 2) rehospitalization at any time after the initial surgery due to adhesions, foreign body, pain, ventral hernia, renal failure, intestinal obstruction or other digestive disorders, urologic/genital disorders within urologic, genital, abdominal or pelvic location.

Cost during and after menorrhagia surgery

We compared the economic impact during and after the surgical management of menorrhagia between strategies over time, by tracking all re-hospitalizations. To do this, we calculated, for each patient, the total cost of hospitalizations, by linking all stays that occurred from the surgery and during a given period of time. For the base-case analysis, the time horizon was fixed at 18 months, as all the included patients had at least 18 months of follow-up, meaning that the total cost can be considered as complete during the period (no cost censoring). Sensitivity analyses were performed with a horizon time of 60 months, only for patients having a follow-up at least equal to 60 months.

Costs were restricted to hospital costs and were determined from the French social security perspective. Hospital costs were calculated using the national DRG tariffs for each year considered, and were expressed in 2017 Euros. Tariffs included nursing care, treatments, drugs, food and accommodation, and investment costs. For public hospitals, tariffs also covered medical and technical procedures. For private hospitals, costs were estimated using the official DRG tariffs for private hospitals to which physician's fees were added (as they are not included in DRG tariffs and are reimbursed on a fee-for-service basis). Whatever the sector, costs also included additional cost per day of hospitalisation in an intensive care unit, if needed. Medications and devices prescribed or delivered during outpatient visits were not considered, as well as ambulatory costs and indirect costs related to productivity loss. Costs are presented as mean cost per patient per strategy.

Statistical analyses and cost-effectiveness study

Categorical data were expressed as proportions, whereas continuous data were expressed as means and standard-deviations (SD).

Both time without failure and time without complications were considered as censored data and were analyzed using a Kaplan-Meier survival method and compared with a log-rank test. For each patient, occurrence of a failure and its delay since the initial menorrhagia surgery were tracked from the initial surgery date until death or last follow-up date (31thDecember 2015). If no failure occurred, the patient was considered as having no failure (censored) at last follow-up date. The occurrence of severe complication was tracked from the initial surgery date until failure, death or last follow-up date (31th December 2015).

The cost-effectiveness analysis was performed comparing each surgical strategy to the 2G one. Groups were both compared in terms of incremental cost (*|euro*) and of incremental effectiveness (*rate of patients without failure*) of the different surgical strategies, as compared to the 2G one, during the 18 months following the initial surgery. Sensitivity analyses were performed by varying the horizon time at 60 months, but the analysis was restricted to the patients with at least this follow-up in the study (as patients with a follow-up less than 60 months may have an underestimation of costs). Secondary analyses were also performed by varying the effectiveness criteria, using the complication rate alone. Analyses were performed by using the R statistical software (version 3.2.3).

Results

Study population

Between 1st January 2009 and 30th June 2014, 152,531 women, 35-55 years old, hospitalized for AUB-O,E,N surgery were identified in the PMSI database, of whom 42,658 presenting at least one exclusion criterion were excluded. The cohort of patients available for analysis thus consisted of 109,873 patients. Of these, 88,154 could be followed for 18 months (Figure 1). In the study population, 5,730 women underwent a 2G surgical procedure (6.5%), 31,437 a 1G procedure (35.7%), 32,304 curettage (36.6%) and 18,647 hysterectomy (21.2%). Mean age of the patients was 46 ± 5.0 years, with no difference between groups.

Effectiveness: patients without failure or complications over time

The rate of patients without failure over time according to each surgical strategy is presented in Figure 2. Hysterectomy was the most effective strategy, as the rate of patients without failure was the highest over time, attaining 97.2% at 18 months and remaining stable until 60 months (Table 2). Conversely, the rate of patients without failure for 2G, 1G and curettage, being 90.1%, 87.3% and 79.4% at 18 months (p<0.0001), showed decrease over time.

The rate of patients without complication over time according to each surgical group is presented in Figure 3. Women undergoing hysterectomy were at significantly higher risk for complications after surgery than

women undergoing 2G procedures (p<0.0001), whereas those undergoing 1G procedures or curettage were at significantly lower risk than patients treated by 2G procedure (p<0.0001).

Economic burden during and after menorrhagia surgery

Table 1 gives the hospitalization costs for initial surgery and during the following 18 months, for the different strategies. Costs were the highest for women having undergone hysterectomy (\euro4,157 per patient on average), almost two-fold higher than for the 2G and curettage (\euro2,448 and \euro2,275 per patient, on average). 1G surgery procedure was the least expensive surgical technique (\euro2,100 per patient), allowing to reduce the hospitalization cost of \euro352 per patient, as compared to 2G.

Cost-effectiveness analysis

The figures 4 and 5 illustrate cost-effectiveness plans, representing the differences both in hospitalization costs and in effectiveness of each surgical procedure at 18 months, compared to the 2G procedure. Effectiveness is expressed as additional percent of patients without failure in figure 4A, and as additional percent of patients without complication in figure 4B.

Hysterectomy is the most effective procedure, as it has the lowest failure rate, but also the most expensive one, with an incremental cost-effectiveness ratio (ICER) estimated at $\langle uro24,008 \pm per additional \%$ of patients without failure at 18 months. It means that, at 18 months following hysterectomy, it is necessary to pay on average patients without failure, as compared to 2G. Hysterectomy was conversely the strategy with the highest complication rate.

Curettage was the least effective procedure, as it was responsible for 20.6% of failure at 18 months, even if it was slightly less expensive than 2G (\euro-177/patient). 1G procedure was also slightly less effective than 2G procedure (-2.8% of patients without failure at 18 months) but was less costly (\euro-352 /patient), leading to an ICER estimated at \euro13,078 per additional % of patients without failure at 18 months. It means that it is possible to gain \euro13,078/patient on average, if we accept to lose one % of success.

Regarding complications at 18 months, hysterectomy was dominated, as this is the strategy with the lowest rate of patients without complication and the more expensive (Figure 5). As compared to 2G, 1G and curet-tage are both slightly more effective (+ 0.4% and +0.5% patients without complication, respectively) and less expensive (\euro-352 and \euro-177 per patient, on average respectively), meaning that these strategies were both dominant.

Discussion

The present study was designed to compare, using a cost-effectiveness analysis, the cost and the effectiveness of four surgical strategies used for the treatment of AUB-O,E,N in France. It showed that mini-invasive 2G and 1G procedures, which are recommended as preferred solutions for the surgical treatment can also be considered as cost-effective procedures, as they are associated with lower severe complication rates and lower costs, when compared to curettage and hysterectomy. Conversely, hysterectomy is the most expensive procedure, because of the high cost of the initial surgery and the higher rate of hospitalization for complications over time; curettage is the least effective one with the highest rate of failures over time.

Our results are in accordance with previous cost-effectiveness studies, confirming that 2G and 1G are costeffective. Our study is the first and the only one for which cost and effectiveness data are entirely extracted from a unique source of data, *i.e.* the PMSI database. Roberts¹⁵ and Garside¹⁶ both point out that theirs models included hypothetical patients and they built them with multiple sources and limited available data. Miller¹⁸ also regrets the incorporation in his model of data from older studies, some of which predate the advent 2G endometrial ablation technologies. Only Fernandez¹³, Bischoff-Everding¹⁷ and Cooper¹⁴ performed their cost analysis using economic data collected on individual patients. These studies are however based on small sample of patients (147, 88 and 660 patients, respectively), which may not be representative of AUB surgical management. Our study has the advantage of being based on observed cost and efficiency data from patients in real-life conditions, in the largest and exhaustive cohort of French patients, over a long observation period. The analysis with KM curves allows considering the time of occurrence of events since the initial surgery in patients with heterogeneous follow-up time. Indeed, the sensitivity analysis based on patients with 60 months of follow-up confirmed the conclusions at 18 months, demonstrating the robustness of our results.

The use of the PMSI database for performing a cost-effectiveness analysis presents other advantages. Since it is the basis of prospective hospital funding, hospitals have to produce standardized reports for each stay performed. Data extracted from the PMSI then presented a high exhaustiveness (all public and private hospitals are included and no sampling is done) and a high level of quality, with limited coding errors. The large number of cases documented allowed the study outcomes to be determined with high precision. Bias due to sampling errors and to loss to follow-up should be minimal. The economic burden of AUB is also expected to be well documented, as the management of the initial surgery and of severe complications occurred in hospital setting. At the time of study completion, hospital external activity was not available in the PMSI database: activity such as consultations or some procedures could not be tracked. Therefore, failure and complications that would have occurred out of hospital and that would not have led to hospitalization shall not have been tracked as they are not reported in the PMSI database. We might have an overestimation of failure/complications avoided. A linkage is currently available between the PMSI and SNIIRAM (French sick funds comprehensive reimbursement database). However, SNIIRAM could not be used in this study, as its access was not possible within the study delay. Other costs could therefore not be tracked, such as sick leaves, leading to potential underestimation of associated costs. However, the overestimation of effectiveness as well as the underestimation of costs might not be different between the 4 groups.

1G and 2G appear to be the preferred techniques. The cost of the device could be offset by its greater use with a logical reduction in the purchase cost and by the economy of occupying operating theaters because performing 2G surgery is twice as fast as for 1G.

In conclusion, this study based on the largest cohort of patients surgically treated for AUB-O,E,N confirms that 1G and 2G techniques are the most efficient strategies in real-life conditions. Despite the fact that hysterectomy and curettage are not recommended as first line strategies, that curettage is the least effective strategy and hysterectomy the most expensive one, both strategies are still used in more than half patients as first line surgical treatment. Switching to 2G techniques would not require a specific training for surgeons, when compared to curettage or hysterectomy, and it would decrease the annual AUB budget impact of about 65 millions \euro (as the extra-cost of hysterectomy compared to 2G is 24,008 \euro and 3000 annual hysterectomies are done in France with 90% of which are not justified for this indication). Improving the 2G French tariffs could foster this switch, allowing a more adapted treatment to these patients, with a limited expected increase of costs for the National Health Insurance. Moreover, most second-generation endometrial ablation are still performed under general or epidural anaesthetic in an operating theatre. However, the new small diameter devices should encourage movement of minimal invasive surgery out of the traditional operating theatre and this next development will accentuate the cost-effectiveness of the treatment of heavy menstrual bleedings by 2G techniques.

Finally, we are at a turning point where we have to balance the superior efficiency of radical surgeries (total or subtotal hysterectomy) and the lesser efficiency of 2G or 1G techniques, but despite all, that being significant with less than 20% reoperations, and their economic impact for national health insurance.

Disclosure of interests : GD, JF, DT, PD, HF and IB received personal fees from Hologic for their participation to Steering Committee during the work. PD, HF and DT reports personal fees from HOLOGIC France, outside the submitted work. HEVA works with all pharmaceutical and medical devices industries like JANSSEN, BMS, PFIZER, NOVARTIS, BSCI. JF reports personal fees from HEVA during the conduct of the study and personal fees from Astellas Pharma outside the submitted work. IB received personnel fees from Novartis, Allergan, CSL-Berhing, Merck outside the submitted work.

Contributions of authorship : This study was initiated by LdL, LL, IB and supported by Hologic. IB, LDL and LL elaborated the protocol. TL and GC performed the PMSI data extraction, their data-management

and their statistical analysis under the control of LL and LDL. IB performed the cost-effectiveness analysis. GD, HF, DT, PD and JF were members of the Steering Committee which oversaw the implementation of the study and contributed to the interpretation of the study. The authors were fully responsible for all content and editorial decisions. All the authors made substantial contributions during all the stages of the work, including the conception and design of the work, acquisition, analysis and interpretation of data, manuscript development, revision of the manuscript and have approved its final version.

Details of ethics approval : The study was conducted in accordance with relevant international and French regulatory requirements. Since this was a retrospective study of an anonymized database and had no influence on patient care, ethics committee approval was not required. Use of the PMSI-MCO database for this type of study has been approved by the French national data protection agency (CNIL; annual authorization #1419102 v7 – 2015-111111-56-18 / order M14N056 and M14L056).

Funding: The study was funded by Hologic (no grant number), a company that markets NovaSure[®], a radiofrequency endometrial ablation device. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

REFERENCES

1 Liu Z, Doan Q V., Blumenthal P, Dubois RW. A systematic review evaluating health-related quality of life, work impairment, and health-care costs and utilization in abnormal uterine bleeding. Value Heal. 2007; 10: 183–94.

2 Karlsson TS, Marions LB, Edlund MG. Heavy menstrual bleeding significantly affects quality of life. Acta Obstet Gynecol Scand2014; 93 : 52–7.

3 Duckitt K. Managing perimenopausal menorrhagia. Maturitas. 2010;66: 251-6.

4 Fraser IS, Mansour D, Breymann C, Hoffman C, Mezzacasa A, Petraglia F. Prevalence of heavy menstrual bleeding and experiences of affected women in a European patient survey. *Int J Gynecol Obstet* 2015;**128** : 196–200.

5 Munro MG, Critchley HOD, Fraser IS, *et al.* The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *Int J Gynecol Obstet* 2018. DOI:10.1002/ijgo.12666.

6 National Collaborating Centre for W, Children's H. National Institute for Health and Clinical Excellence: Guidance. In: Heavy Menstrual Bleeding. 2007.

7 Marret H, Fauconnier A, Chabbert-Buffet N, *et al.* Clinical practice guidelines on menorrhagia: Management of abnormal uterine bleeding before menopause. Eur. J. Obstet. Gynecol. Reprod. Biol. 2010;**152** : 133–7.

8 Cooper K, Lee AJ, Chien P, Raja EA, Timmaraju V, Bhattacharya S. Outcomes following hysterectomy or endometrial ablation for heavy menstrual bleeding: Retrospective analysis of hospital episode statistics in Scotland. *BJOG An Int J Obstet Gynaecol* 2011. DOI:10.1111/j.1471-0528.2011.03011.x.

9 Kroft J, Liu G. First-Versus Second-Generation Endometrial Ablation Devices for Treatment of Menorrhagia: A Systematic Review, Meta-Analysis and Appraisal of Economic Evaluations. J Obstet Gynaecol Canada2013; **35** : 1010–9.

10 Lethaby A, Penninx J, Hickey M, Garry R, Marjoribanks J. Endometrial resection and ablation techniques for heavy menstrual bleeding. Cochrane Database Syst. Rev. 2013; **2013** . DOI:10.1002/14651858.CD001501.pub4.

11 Daniels JP, Middleton LJ, Champaneria R, *et al.* Second generation endometrial ablation techniques for heavy menstrual bleeding: network meta-analysis. BMJ. 2012; **344**. DOI:10.1136/bmj.e2564.

12 Cooper K, McCormack K, Breeman S, *et al.* HEALTH: Laparoscopic supracervical hysterectomy versus second-generation endometrial ablation for the treatment of heavy menstrual bleeding: Study protocol for a randomised controlled trial. *Trials* 2018. DOI:10.1186/s13063-017-2374-9.

13 Fernandez H, Kobelt G, Gervaise A. Economic evaluation of three surgical interventions for menorrhagia. *Hum Reprod* 2003;**18** : 583–7.

14 Cooper K, Breeman S, Scott NW, et al. Laparoscopic supracervical hysterectomy compared with secondgeneration endometrial ablation for heavy menstrual bleeding: The HEALTH RCT. Health Technol Assess (Rockv) 2019. DOI:10.3310/hta23530.

15 Roberts TE, Tsourapas A, Middleton LJ, *et al.* Hysterectomy, endometrial ablation, and levonorgestrel releasing intrauterine system (Mirena) for treatment of heavy menstrual bleeding: Cost effectiveness analysis. In: BMJ (Online). 2011. DOI:10.1136/bmj.d2202.

16 Garside R, Stein K, Wyatt K, Round A, Pitt M. A cost-utility analysis of microwave and thermal balloon endometrial ablation techniques for the treatment of heavy menstrual bleeding. *BJOG An Int J Obstet Gynaecol* 2004; **111** : 1103–14.

17 Bischoff-Everding C, Soeder R, Neukirch B. Economic and clinical benefits of endometrial radiofrequency ablation compared with other ablation techniques in women with menorrhagia: A retrospective analysis with German health claims data. Int J Womens Health 2016;8: 23–9.

18 Miller JD, Lenhart GM, Bonafede MM, Basinski CM, Lukes AS, Troeger KA. Cost effectiveness of endometrial ablation with the NovaSure® system versus other global ablation modalities and hysterectomy for treatment of abnormal uterine bleeding: US commercial and medicaid payer perspectives. *Int J Womens Health* 2015; **7**: 59–73.

19 Bezin J, Duong M, Lassalle R, *et al.* The national healthcare system claims databases in France, SNIIRAM and EGB: Powerful tools for pharmacoepidemiology. *Pharmacoepidemiol Drug Saf* 2017;**26** : 954–62.

20 WHO. International Statistical Classification of Diseases and Related Health Problems (International Classification of Diseases)(ICD) 10th Revision - Version:2010. 2010.

21 de Léotoing L, Chaize G, Fernandes J, *et al.* The surgical treatment of idiopathic abnormal uterine bleeding: An analysis of 88 000 patients from the French exhaustive national hospital discharge database from 2009 to 2015. *PLoS One* 2019. DOI:10.1371/journal.pone.0217579.

Table 1: Hospitalization costs and rate of patients without failure and without complication, over 18 months, for the different surgical strategies

	$2{ m G}~{ m surgery} \ { m N}{=}5~730~{ m pts}$	$1{ m G}~{ m surgery} \ { m N}{=}31~473~{ m pts}$	Curettage N=32 304 pts	${f Hysterectomy} \ {f N=18} \ 647 \ { m pts}$
Hospitalization costs	Hospitalization costs	$\begin{array}{c} \text{Hospitalization} \\ \text{costs} \end{array}$	Hospitalization costs	Hospitalization costs
Mean cost per	$2\ 448\ \pm\ 8254\ [2234;$	2100 ± 3476 [2061;	$2\ 275\pm 5\ 278\ [2217;$	$4\ 157 \pm 3\ 535\ [4106;$
patient at 18 months	2661]	2138]	2332]	4208]
Difference of cost as compared to 2G strategy	-	$-352 \pm 115 \ [-359;$ -345]	-177 ± 115 [-185; -170]	$1705 \pm 115 [1697; 1712]$
Failure	Failure	Failure	Failure	Failure
Rate of patients without failure at 18 months	90.1% [89.3-90.8]	87.3% [86.9-87.6]	79.4% [79.0-79.9]	97.2% [97.0;97.5]

	$2{ m G}~{ m surgery} \ { m N}{=}5~730~{ m pts}$	1G surgery N=31 473 pts	$egin{array}{c} { m Curettage} \ { m N=32} \ 304 \ { m pts} \end{array}$	${ m Hysterectomy} \ { m N}{ m = 18} \ { m 647} \ { m pts}$
Difference in the proportion of patients without failure at 18 months, as compared to 2G	-	-2.8% [-2.8 ; -2.8]	-10.6% [-10.7 ; -10.6]	+7.1% [7.1 ; 7.2]
Complication Proportion of patients without complication at 18 months	Complication 97.9% [97.5-98.3]	Complication 98.3% [98.1-98.4]	Complication 98.4% [98.3-98.6]	Complication 94.2% [93.9;94.6]
Difference in the proportion of patients without complication at 18 months, as compared to 2G	-	$+0.4\%\;[0.4\;;0.4]$	$+0.5\%\;[0.5\;;\;0.5]$	-3.7% [-3.7 ; -3.7]

Table 2: Hospitalization costs and rate of patients without failure and without complication, over 60 months, for the different surgical strategies for the 33 093 patients with at least 60 months of follow-up

	2G surgery N=1 676 pts	$1{ m G}~{ m surgery} \ { m N}{=}11\ 084\ { m pts}$	${ m Curettage} \ { m N=13} \ { m 335} \ { m pts}$	${f Hysterectomy}\ {f N=6}$ 998 pts
Hospitalization	Hospitalization	Hospitalization	Hospitalization	Hospitalization
costs	costs	costs	costs	costs
Mean cost per	$4\ 438\ \pm\ 7610$	$4071 \pm 7243 \ [3936;$	$4\ 277 \pm 8\ 553\ [4132;$	$6\ 435\pm 8\ 530\ [6235;$
patient at 60	[3936-4206]	4206]	4422]	6635]
months	t j	Ĩ	,	1
Difference of cost	-	$-367 \ensuremath{\setminus euro}$	-161 \euro	$+1997$ \euro
as compared to		Υ.	,	Υ.
2G strategy				
Failure	Failure	Failure	Failure	Failure
Rate of patients	80.3% [78.4-82.2]	77.5% [76.7-78.3]	68.5% [67.7-69.3]	97.2% [96.8; 97.6]
without failure at	L J	L J	. ,	L , J
60 months				
Difference in the	-	-2.8%	-11.8%	+16.9%
proportion of				
patients without				
failure at 18				
months, as				
compared to 2G				
Complication	Complication	Complication	Complication	Complication
Proportion of	94.2% [93.0-95.3]	96.1% [95.8-96.4]	96.3% [95.9-96.6]	89.4% [88.7-90.2]
patients without	01.270 [00.0 00.0]	00.170 [00.0 00.1]	00.070 [00.0 00.0]	00.170 [00.1 00.2]
complication at 60				
months				
1110110115				

	$2{ m G}~{ m surgery} \ { m N}{=}1~676~{ m pts}$	1G surgery N=11 084 pts	$egin{array}{c} { m Curettage} \ { m N}{=}13 \ 335 \ { m pts} \end{array}$	${f Hysterectomy}\ {f N=6}$ 998 pts
Difference in the proportion of patients without complication at 60 months, as compared to 2G	-	+1.9%	+2.1%	-4.8%

List of figures :

Figure 1: Flow-chart of patients selected for study

Figure 2: Time without failure over time according the initial surgical groups

Figure 3: Time without complication over time according to the surgical groups

Figure 4: Cost-effectiveness plan

A - representing the difference of cost and the additional rate of patients without failure of the surgical procedures at 18 months, compared to the 2G groupB- representing the difference of cost and the additional patient without complication of the surgical procedures compared to the 2G \rm

Online supporting material 1: CCAM codes for menorrhagia surgery

CCAM code	French title
$\overline{2G}$ (2 nd generation endometrial ablation techniques such as radiofrequency, laser)	$2G (2^{nd} \text{ generation endometrial abla})$
JKND001	Destruction de la muqueuse utérine
1G $(1^{st}$ generation endometrial ablation techniques, such as loop resection)	$1 \text{G} (1^{\text{st}} \text{ generation endometrial abla})$
JKNE001	Abrasion de la muqueuse de l'utérus
Curettage	Curettage
JKGD002	Curetage de la cavité de l'utérus à v
JKQE001	Hystéroscopie avec curetage de la ca
JKGD003	Curetage de la cavité de l'utérus à v
Hysterectomy	Hysterectomy
JKFC002	Hystérectomie subtotale, par cœlios
JKFC006	Hystérectomie subtotale avec annex
JKFC005	Hystérectomie totale, par cœlioscopi
JKFA018	Hystérectomie totale, par cœlioscopi
JKFA026	Hystérectomie totale, par abord vag
JKFC003	Hystérectomie totale avec annexecto
JKFA006	Hystérectomie totale avec annexecto
JKFA005	Hystérectomie totale avec annexecto
JKFA024	Hystérectomie subtotale, par laparo
JKFA032	Hystérectomie subtotale avec annex
JKFA015	Hystérectomie totale, par laparotom
JKFA028	Hystérectomie totale avec annexecto

Online supporting material 2: ICD-10 codes for menorraghia

ICD-10 code	Wording
N800	Endométriose de l'utérus (Adénomyose)
	Endometriosis of uterus
N850	Hyperplasie glandulaire de l'endomètre
	Endometrial glandular hyperplasia
N920	Menstruation trop abondante et trop fréquente
	avec cycle menstruel régulier Excessive and
	frequent menstruation with regular cycle
N921	Menstruation trop abondante et trop fréquente
	avec cycle menstruel irrégulier Excessive and
	frequent menstruation with irregular cycle
N924	Saignements abondants de la préménopause
	Excessive bleeding in the premenopausal period
N925	Autres irrégularités menstruelles précisées Other
	specified irregular menstruation
N926	Irrégularités menstruelles, sans precision Irregular
	menstruation, unspecified
N938	Autres saignements anormaux précisés de l'utérus
	et du vagin Other specified abnormal uterine and
	vaginal bleeding
N939	Saignement anormal de l'utérus et du vagin, sans
	précision Abnormal uterine and vaginal bleeding,
	unspecified

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Figure_5_Borget.docx available at https://authorea.com/users/348247/articles/473696-surgical-treatment-of-abnormal-uterine-bleeding-aub-o-e-n-a-cost-effectiveness-study-using-the-french-hospital-claims-database