



Magnetic Resonance guided Focused ultrasound in uterine fibroids treatment: a cost analysis

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ABSTRACT

Introduction: uterine fibroids are the most common benign tumors of reproductive-age women. Different treatment options exist such as myomectomy, hysterectomy, drugs and uterine artery embolization (UAE). Recently, technological progress provides non-invasive and conservative treatments such as MRgFUS (Magnetic Resonance-guided Focused Ultrasound Surgery).

Objective: the aim of this study was to estimate the mean cost per treatment with MRgFUS.

Methods: cost analysis was performed from the hospital perspective. Total costs were considered. They were defined as the sum of fixed costs (equipment and maintenance costs) and variable costs (personnel, materials and drugs costs). A deterministic approach was followed assuming that all patients require an equal resources utilization. The average materials and drugs consumption was quantified by reviewing medical records of patients treated and through experts' opinion. Cost data were provided by the hospital accounting office.

Results: the mean cost of a single treatment with MRgFUS was equal to € 2.101,85, lower than the DRG tariffs paid for alternative treatments.

Conclusions: the MRgFUS could be an evaluable alternative to standard techniques, as it would allow an immediate improvement in patients' quality of life and cost savings for the hospital as well as for healthcare system.

Keywords: MRgFUS, uterine fibroids, costs, cost analysis.

SOMMARIO

Introduzione: i fibromi uterini costituiscono la forma più diffusa di tumore benigno nelle donne in età fertile. Esistono diverse opzioni di trattamento quali miomectomia, isterectomia, trattamenti farmacologici ed embolizzazione dell'arteria uterina. Negli ultimi anni il progresso scientifico punta sempre di più all'uso di tecniche sempre meno invasive e più conservative tra le quali l'MRgFUS (Magnetic Resonance-guided Focused Ultrasound Surgery).

Obiettivo: stimare il costo medio di un singolo trattamento tramite MRgFUS.

Metodi: la valorizzazione delle risorse utilizzate è stata effettuata secondo la prospettiva dell'ospedale. Sono stati considerati i costi totali definiti come somma dei costi fissi (costo delle apparecchiature e delle manutenzioni) e dei costi variabili (costo del personale, dei materiali e dei farmaci). È stato seguito un approccio deterministico ipotizzando che tutti i soggetti trattati comportino un uguale uso di risorse. Il consumo medio di materiali e farmaci è stato quantificato mediante l'opinione di personale medico. I dati di costo sono stati forniti dall'ufficio contabilità e bilancio dell'ospedale.

Risultati: il costo medio di un trattamento con MRgFUS pari € 2.101,85 risulta inferiore alle tariffe previste dai DRG per i trattamenti alternativi.

Conclusioni: l'MRgFUS potrebbe essere una valida alternativa alle tecniche standard, in quanto permetterebbe un miglioramento immediato della qualità di vita delle pazienti e un possibile risparmio di costi per il sistema sanitario.

INTRODUCTION

Uterine fibroids are the most common benign tumors in women in reproductive-age. In Italy, the diagnosed fibroids prevalence equals 23.6%⁽¹⁾. Common symptoms are abnormal vaginal bleeding, abdominal pressure, urinary or bowel discomfort, back pain and reproductive dysfunction. Diagnosis is based on clinical signs and gynecological examination which allows evaluating the increase in uterine volume, the degree of mobility and the possible site of myomatous nodule.

Diagnostic imaging allows a precise determination of fibroids' location and number. In addition, ultrasound examination usually provides all the necessary information to therapeutic planning, but magnetic resonance imaging (MRI) is necessary in particular cases. MRI, although more expensive than ultrasound examination, is more sensitive, less operator-dependent and very precise in both location of fibroids and identification of stalked fibroids. MRI allows the diagnosis and the study of other pelvic pathologies, such as adenomyosis, which could modify treatment strategies and increase surgical risk⁽²⁾. Imaging, therefore, is essential to confirm or rule out the diagnosis and to select the most appropriate and effective therapeutic strategy.

Treatment options for symptomatic uterine fibroids include conservative (myomectomy) or radical (hysterectomy) surgery, drugs and uterine artery embolization (UAE). In recent years, the MRgFUS (Magnetic Resonance-Guided Ultrasound Surgery), a new non-invasive technique in the treatment of uterine fibroids, is emerging at a local and international level. This technique is based on the application of a focused ultrasound surgery (FUS) under real-time MRI guidance and control⁽³⁾. Treatment is performed transcutaneously in a state of conscious sedation in order to have a constant feedback from the patient during the procedure. The FUS produces coagulative necrosis in a precise focal point (sonication) through a rapid increase of local temperature (60-80 °C) with a fibroid volume reduction relieving from the pathology associated symptoms⁽³⁾. The innovation consists in the ability to monitor in real time the temperature variations of trading volumes and tissues crossed by the ultrasound. MR images are acquired before, during and after the session. Information from images are essential to plan treatment, to identify target volumes, to monitor in real time the evolution of the temperature and to find the exact point of ablation and distribution of the thermal dose.

In 2004, the United States Food and Drug Administration (FDA) approved the MRgFUS⁽⁴⁾, which obtained CE mark in 2007 and was recommended in United Kingdom (UK) by NICE (National Institute for Clinical Excellence) for uterine fibroids treatment in 2011. In Italy, the technique is being tested in five specialized centers such as Niguarda Ca' Granda Hospital in Milan, Umberto I University Hospital in Rome, San Salvatore Hospital in L'Aquila, San Raffaele G. Giglio Hospital in Cefalù and P. Giaccone University Hospital in Palermo. The adoption of a new technology in healthcare is the result of a complex process that involves researchers, citizens, public institutions and industry. In recent decades, the widespread of highly costly innovative technologies and the increasing costs of research and development have been raising questions about the financial sustainability of healthcare systems. The major challenge for decision makers is to face potentially unlimited healthcare needs relying on limited resources availability. Therefore, it is essential to balance the need for a fair acknowledgement of the value of new technologies, on the one hand, and the request for costs containment on the other hand.

Currently, a few studies have investigated the cost-effectiveness of MRgFUS versus the standard practice, showing that MRgFUS therapy results as a dominant strategy being characterized by lower costs and higher benefits. Results from a study conducted in the UK⁽⁵⁾ show that MRgFUS is cost-saving compared to the alternative treatments, yielding an average saving of about £295 per patient. Taking into account indirect costs, savings rise to more than £500 for each woman treated. A significant increase in benefits for patients in terms of QALYs (Quality Adjusted Life Years) is associated with this cost saving. In the U.S. study conducted by O'Sullivan et al. in 2009⁽⁶⁾, the annual cost of uterine fibroids has been estimated at \$2.2 billion and the MRgFUS proves to be a cost-effective technology.

Scientific evidence currently available suggests that MRgFUS exhibits equal or superior efficacy than alternative treatments, in addition to relevant advantages of allowing rapid symptoms remission and being mini invasive technique. However, being an innovative technology not yet codified in any Regional Health Care Range of Fees, MRgFUS needs a careful evaluation of costs and benefits, in order to encourage rational and well-informed decisions. At the moment, there are no studies and cost analyses of MRgFUS in Italy.

Given this background, the aim of this study was to conduct a cost analysis in order to provide information on costs and potential savings associated with fibroids MRgFUS treatment in the Italian context.

MATERIALS AND METHODS

The cost analysis was performed from a hospital perspective and resource consumption was quantified taking into account costs actually incurred by the health facility. Data on treatment time and drugs consumption were derived from medical records of patients treated. Disposables consumption has been identified and quantified through experts' opinion. Cost data were provided by the accounting office of San Raffaele Giglio hospital in Cefalù, Sicily. Total costs defined as the sum of fixed costs (equipment and maintenance) and variable costs (staff, supplies and drugs) were considered in the analysis. A deterministic approach was followed, assuming that costs are not patient-specific but equal for all patients, that is, all patients give rise to the same resource use. The equipment cost was the most relevant item among fixed costs. San Raffaele-Giglio Hospital utilizes the ExAblate 2100 system, by InSightec company. The ExAblate system consists of a patient mobile table and an emission and conduction system of ultrasound beam placed inside a last generation magnetic resonance (MR) GE Sigma HDtx. A workstation is used for planning and remote execution of treatment from the control room. Moreover, an emergency button inside can be used by the patient to report any problems during the treatment session.

In order to compute the equipment cost per procedure, the number of treatments potentially feasible in one year was calculated by keeping in account work shifts, department logistic and needs and the annual depreciation rate was first calculated for the dedicated equipment, assuming that these devices have an average life cycle of 8 years. Since the MRgFUS system includes an ultrasound ExAblate 2100 and a MR GE Sigma HDTX, the depreciation for the two technologies was calculated separately. The depreciation rate per procedure for the device totally dedicated to MRgFUS treatment (ExAblate 2100) was obtained by dividing the annual depreciation rate by the number of procedures potentially feasible each year. With regard to the non-dedicated equipment (MR), the annual depreciation rate was divided by the total number of hours of equipment use so that the rate allocated to MRgFUS session

was calculated on the basis of the number of hours devoted to MRgFUS treatments. The cost of maintenance per procedure was estimated through the same method.

Staff costs refer to the cost of professional figures involved in the treatment of uterine fibroids with MRgFUS: radiologist, anesthesiologist, health physicist, nurse and radiology technician. For every unit of staff, costs were calculated based on their hourly wage (including direct and indirect charges), obtaining €49/h for the radiologist, €45/h for the anesthesiologist, €37,66/h for health physicist, €23,39/h for the nurse, €27,84/h for the radiology technician. The resulting hourly cost was then multiplied by the mean treatment time for each staff unit, as estimated on the basis of experience and evidences. As a result, the cost of each professional profile and overall staff cost was obtained. The duration of treatment of uterine fibroids with MRgFUS varies between 3 and 6 hours and depends mainly on the size of the fibroids and subjective parameters such as the threshold of tolerance of pain or the anxiety of the patient. For the purpose of this study an average duration of 4 hours per treatment was assumed, including the phase of preparation of the patient before surgery and discharge procedures.

Supply costs included all the materials used for each procedure (from patient positioning to discharge) and therefore included anesthetic drugs, medical contrast mediums, dressing materials and other disposable items (gloves, coats, syringes, catheters and disposable kits). Dosage of drugs administered during the treatment was quantified by consulting medical records of the patients treated and through experts' opinion. Data on anesthetic drugs consumption were derived from medical records of patients previously treated, and the average consumption was quantified according to experts' opinion. Drugs and supplies cost for each treatment was obtained by multiplying their unit cost by estimated average consumption. Overhead expenses were assumed equal to 20% of total costs of MRgFUS treatment. Training cost of technical staff and follow up costs were not considered in the analysis.

RESULTS

To evaluate the mean cost per procedure, we considered equipment costs, staff, drugs and supplies costs. The overall equipment costs of € 1.854.846,20 for MRgFUS and € 2.034.000 for MR, include the cost of acquisition, as well as maintenance and upgrades.

Table 1.
Equipment costs.

MRgFUS	Unit cost
Acquisition	€ 1.500.000,00
Upgrade	€ 280.000,00
Annual Maintenance	€ 74.846,20
MR	
Acquisition	€ 1.440.000,00
Upgrade	€ 504.000,00
Annual Maintenance	€ 90.000,00

Table 2.
Staff cost per hour.

Staff	Cost/hour
Radiologist	€ 49,01
Anesthetist	€ 44,98
Health physicist	€ 37,66
Radiology technician	€ 27,84
Nurse	€ 23,39

Table 3.
Supplies and drugs cost.

Supplies and drugs	Average consumption	Unit cost
Kit FUS	1	€ 338,40
Venous catheter	1	€ 0,21
Saline solution 500 ml	1,5	€ 0,90
Sterilecoats	1	€ 0,42
Disposable razor	1	€ 0,10
Syringe 10 ml	1	€ 0,05
Syringe 60 ml	4,5	€ 0,75
Eco-bottle gel	2	€ 0,75
Endorectal catheter	1	€ 0,12
Connector drip	1	€ 0,10
Paper roll	1	€ 1,46
Disposable gloves	6	€ 0,19
Medical Contrast medium (Gadovist)	6,5 mg	€ 33,00
Diazepam/Midazolam	5 mg	€ 0,24
Fentanest/Propofol	5 mg	€ 0,70
Pethidine	5 mg	€ 0,31

These cost items are reported in **Table 1**. Staff costs refer to hospital cost per hour including social charges (**Table 2**). Staff cost is a fixed cost for the hospital, but it could be considered variable in the current analysis since the share of cost per procedure depends on the duration of treatment.

The cost of drugs and materials was obtained

based on the estimated average consumption for each treatment. Supplies and drugs used are listed in **Table 3** including their average consumption and unit costs. MRgFUS treatment requires a low consumption of materials and drugs: only the disposable KIT FUS is the most considerable cost driver in this category.

Table 4.
Mean cost per treatment.

Cost items	Mean cost per procedure
Equipment	
MRgFUS depreciation charge	€ 285,26
MR depreciation charge	€ 233,65
MRgFUS maintenance	€ 71,97
MR maintenance	€ 86,54
Equipment cost	€ 677,42
Staff	
Radiologist	€ 196,05
Anesthetist	€ 179,91
Health physicist	€ 150,64
Radiology technician	€ 111,35
Nurse	€ 58,47
Staff cost	€ 696,42
Supplies	
Kit FUS	€ 338,40
Drugs	€ 34,25
Consumables	€ 5,06
Supplies cost	€ 377,71
Mean cost per treatment	€ 1751,55
Overheads	€ 350,31
Total mean cost per treatment	€ 2101,85

Finally, the current cost-analysis resulted in an overall cost of € 2.101,85 for MRgFUS treatment. The mean costs per procedure are summarized in **Table 4**.

DISCUSSION

Uterine fibroids have a negative impact on the National Health Service budget in terms of

costs of visits, hospitalizations and treatments. Considering the societal perspective the disease also imposes high costs to the general population in terms of absenteeism and productivity losses. In a cross-sectional study conducted on 1756 women from five European countries including Italy⁽¹⁾, 19.6% of Italian women reported to have been hospitalized. Of these more than 30% received pharmacological or surgical treatments. Uterine fibroids are traditionally treated surgically. Surgical approaches are usually associated with intra operative complications such as bleeding, deformation of the uterine cavity, risk of emergency hysterectomy and subsequent uterine rupture in future pregnancies⁽⁷⁾. MRgFUS is an innovative technology in radiology for the local treatment of tumor lesions with the advantage of preserving the surrounding healthy tissues. In Italy, this procedure has not been codified yet in any Regional Health Care Range of Fees and, therefore, patients enrollment in clinical trials is still limited.

The MRgFUS procedure was initially approved by FDA for premenopausal women with symptomatic fibroids who had no desire for future fertility. However, a few years later, based on the experience accrued in the field of MRgFUS and a deeper understanding of outcomes in pregnant women, the FDA amended the labeling of the device recommending to take into account desire for future pregnancy but not to consider this as an absolute contraindication. Women who desire further fertility can undergo MRgFUS since 2007⁽⁸⁾. There is some scientific evidence on safety and efficacy of this technique in terms of lesion reduction, remission of symptoms and improved patients' quality of life^(3,9-13). In particular, two studies show a 33% volume reduction and significant symptoms improvement six months after MRgFUS^(11, 12). Recent studies⁽¹⁴⁾ on effectiveness of MRgFUS report a percentage of non-perfused volume (NPV) of 98%⁽³⁾, 80%⁽¹⁵⁾, 90%⁽¹⁶⁾, 90%⁽¹⁷⁾ and 88%^(18,19). Moreover, an average rate of NPV greater than 70% was observed during 15 treatments carried out at San Raffaele Giglio hospital. In addition, several analyses⁽²⁰⁻²⁶⁾ describe the effect of treatment on fertility (when this problem is associated with fibroids); in particular, Rabinovici et. al⁽²⁷⁾ reports findings of an high successful pregnancies rate after MRgFUS. Concerning re-intervention rates, one non-randomized study reported a rate of 4% at 6 months follow-up⁽¹³⁾, whereas re-intervention rates range between 5% and 10% in studies with 12 months follow-up^(28, 29) and between 14% and

21.6% at month 24⁽³⁰⁾. A re-intervention rate of 15% was recorded during a study with 34 months follow-up period⁽²⁸⁾. Kim et al.⁽³¹⁾ reported that 69% of patients did not need a second surgery three years after MRgFUS, while a study conducted in Germany⁽³²⁾ from 2002 to 2009 shows a re-intervention rate of 66% after 60 month follow-up. Finally, the innovative technology is associated with fewer adverse events and complications than the myomectomy, as well as with a reduction of hospital stay and a rapid return to usual activities^(7, 8, 28).

As all innovative technologies, MRgFUS has relevant costs of investment and management against benefits previously described. In the present work, overall costs associated with MRgFUS treatment were quantified as the sum of fixed costs (equipment and maintenance) and variable costs (staff and supplies costs). The staff is multidisciplinary and highly specialized: medical personnel, nurses and technicians involved during pre-treatment, treatment and follow-up phases.

Our cost analysis estimates a cost per procedure of 2,100 Euro. An average duration of four hours per procedure was hypothesized, although some sources indicate a shorter duration, from two to three hours per session⁽⁸⁾, so that the cost per procedure could be lower. The estimated cost per MRgFUS procedure is lower than the Diagnosis Related Group (DRG) tariffs used for alternative therapies. More in detail, we can consider DRG tariffs 354 and 355 related to intervention on uterus and adnexa not for malignant neoplasm with or without complications, respectively, and DRG number 356 about female reproductive system reconstructive procedures⁽³³⁾. DRG tariff 356, equal € 2.901, being the lowest value among three DRG tariffs considered, but it is still higher than the cost of MRgFUS in uterine fibroids treatment herein estimated. Also the average value of these tariffs (€3.415) is more than 1,000 higher than our result.

MRgFUS is a minimally invasive technique that allows patients to avoid intraoperative and post-surgical risks, to get total symptoms remission and to become pregnant if they are in reproductive-age.

This technique allows a maximization of available resources because it can be performed in a single session in outpatient setting. Evidence from the literature and our cost analysis suggest that focused ultrasound treatment results in an improvement in symptoms and patients' quality of life and eventually in a cost saving for National Health Service. The use of an innovative technology like MRgFUS is usually associated with a lack of long-term data on efficacy and safety. In addition, although several preclinical studies on FUS treatments have been carried out, this option has not yet been studied in women with uterine fibroids within an experimental setting. Moreover, several analyses compare findings from women treated with uterine artery embolization (UAE) with conventional surgical procedures, but there are no studies that compare MRgFUS treatment with other conventional techniques. Even though international literature demonstrates the cost-effectiveness of MRgFUS, economic evaluations should be performed also in Italy, since resource consumption data are scarcely transferable from foreign contexts. This would allow to develop context-specific to comparisons of benefits and costs associated with MRgFUS with those of standard techniques, such as myomectomy, in order to inform decisions at a local or hospital level. Further developments of this research could concern long-term benefits and costs, including in the analysis follow-up costs (hospitalizations, visits) and indirect costs of absenteeism and productivity losses. Finally, our analysis is based on a small sample of patient in a single medical center, so it would be preferable to extend the analysis to the rest of the Italian medical centers in order to obtain more generalizable and representative results.

DISCLOSURE

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