Saline infusion sonohysterography

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The Secretary
Medicare Services Advisory Committee
Department of Health and Aged Care
Mail Drop 107
GPO Box 9848
Canberra ACT 2601

Enquiries about the content of the report should be directed to the above address.

The Medicare Services Advisory Committee is an independent committee which has been established to provide advice to the Commonwealth Minister for Health and Aged Care on the strength of evidence available on new medical technologies and procedures in terms of their safety, effectiveness and cost-effectiveness. This advice will help to inform Government decisions about which new medical services should attract funding under Medicare.

This report was prepared by the Medicare Services Advisory Committee (MSAC). The report was endorsed by the Commonwealth Minister for Health and Aged Care on 11 May 1999.

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MSAC recommendations do not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

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Saline infusion sonohysterography (SIS) is a diagnostic procedure that enhances endometrial imaging by using saline as a contrast medium. It has been used in conjunction with traditional transvaginal ultrasound to aid the diagnosis of uterine and endometrial abnormalities, including abnormal uterine bleeding, infertility, recurrent abortion, suspected Ashermann's syndrome, and patients receiving tamoxifen therapy.

Medicare Services Advisory Committee — role and approach

The Medicare Services Advisory Committee (MSAC) is a key element of a measure taken by the Commonwealth Government to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Minister for Health and Aged Care on the evidence relating to the safety, effectiveness and cost-effectiveness of new medical technologies and procedures, and under what circumstances public funding should be supported.

A rigorous assessment of the available evidence is thus the basis of decision making when funding is sought under Medicare. The medical literature available on the technology is searched and the evidence is assessed and classified according to the National Health and Medical Research Council (NHMRC) four-point hierarchy of evidence. A supporting committee with expertise in this area then evaluates the evidence and provides advice to MSAC.

MSAC's assessment of SIS

For SIS, the search of the medical literature available on the role of SIS in the diagnosis of abnormal uterine bleeding revealed only one 'head-to-head' randomised controlled trial, which was a trial of SIS and transvaginal ultrasound (TVS). However, although providing some additional information on SIS, this trial does not reflect the proposed clinical use of the procedure in Australia. The remaining 13 studies presented level III-2 evidence (comparative studies with concurrent controls, where allocation is not randomised; case-control studies; or interrupted time-series, with a control group).

Clinical need

Abnormal uterine bleeding is a common complaint in routine gynaecological practice. There are several underlying conditions that can cause this problem, some of which can be life-threatening. It is important that the presence of endometrial carcinoma is diagnosed early and accurately, as it is the most common cancer of the female reproductive system, 90% of cases occurring in women aged over 50.

Safety

When used in conjunction with TVS, SIS is a safe procedure, with a low incidence of minor complications (level III-2 evidence).

Effectiveness

SIS, when used in conjunction with TVS, has a higher sensitivity than TVS alone in the detection of uterine cavity abnormalities, and has a similar specificity (level III-2 evidence). It benefits clinical decision making, as a proportion of patients will avoid diagnostic hysteroscopy.

Cost-effectiveness

SIS is associated with a cost saving due to hysteroscopies avoided. Sensitivity analysis indicates that the incremental cost-effectiveness ratio could be up to $1052 per extra hysteroscopy avoided.

Recommendation

MSAC recommended that on the strength of evidence pertaining to saline infusion sonohysterography, public funding should be supported for this procedure as a second-line diagnostic procedure for abnormal uterine bleeding, when findings from transvaginal ultrasound are inconclusive.

Introduction

The Medicare Services Advisory Committee (MSAC) has reviewed the use of saline infusion sonohysterography (SIS), which is a procedure to aid the diagnosis of uterine and endometrial abnormalities. MSAC evaluates new health technologies and procedures for which funding is sought under the Medicare Benefits Scheme (MBS) in terms of their safety, effectiveness and cost-effectiveness, while taking into account other issues such as access and equity. MSAC uses an evidence-based approach to its assessments, based on reviews of the scientific literature and other information sources, including clinical expertise.

MSAC's terms of reference and membership are at Appendix A. MSAC is a multidisciplinary expert body, comprising members drawn from disciplines such as diagnostic imaging, pathology, surgery, medical administration, internal medicine and general practice, clinical epidemiology and health economics.

This report summarises the assessment of current evidence for the use of SIS as a second-line diagnostic procedure for women with abnormal uterine bleeding.

Background

Saline infusion sonohysterography

How it works

Saline infusion sonohysterography (SIS) enhances endometrial imaging by using saline as a contrast medium. It has been used in conjunction with traditional transvaginal ultrasound (TVS) to aid the diagnosis of uterine and endometrial abnormalities, including abnormal uterine bleeding, infertility, recurrent abortion, suspected Ashermann's syndrome and patients on tamoxifen therapy. The fallopian tubes may also be investigated by SIS.

SIS can be via transvaginal or transabdominal ultrasound examination, but is mainly performed transvaginally. With the aid of a vaginal speculum, the cervix is visualised and after cleansing with aqueous chlorhexidine a catheter primed with saline is passed into the internal os. Using a 20-mL syringe, 3–10 mL sterile saline is injected into the uterine cavity. The uterine cavity is then ultrasonographically examined in both the longitudinal and transverse sections. The procedure takes about 30 minutes, and no special aftercare or antibiotic prophylaxis is routinely required.

The procedure does not require an anaesthetic and can be performed in an outpatient clinic.

Intended purpose

The main proposed use for SIS is as a second-line diagnostic procedure for women with abnormal uterine bleeding, to be used as a second-line diagnostic procedure if an abnormal and/or inconclusive TVS result is obtained.

Clinical need/burden of disease

Abnormal uterine bleeding is a common presenting complaint of women seen in routine gynaecological practice. In the United States, it is estimated that up to 20% of visits to a gynaecologist are for abnormal uterine bleeding.[1] Detailed statistics of abnormal uterine bleeding in Australia are not available. Abnormal uterine bleeding occurs often in both premenopausal and postmenopausal women, and is related to a number of underlying conditions, for example, anovulation, pregnancy problems, hormonal factors, and benign or malignant uterine lesions. Some of these can be life-threatening and/or affect patients' quality of life significantly. It is important that the presence of endometrial carcinoma can be diagnosed early and accurately, as endometrial carcinoma is the most common reproductive cancer, and 90% occurs in women over 50 years of age.[2]

Data on Medicare usage show that during the 1996–97 financial year, 2600 endometrial biopsy (EMB) services (MBS items 35620 and 35622) were used within 30 days of TVS (MBS items 55042 and 55043); the incidence of hysteroscopy (MBS items 35626, 35627 and 35630) given within 30 days of TVS was 6500. Based on the current clinical practice in Australia, the main reason for use of these services was investigation of abnormal uterine bleeding. However, the data collected do not capture the indication for which the services are provided, so it is not possible to reach any verifiable conclusions. As Medicare utilisation data do not include services to public patients provided in public hospitals, these figures provided an incomplete picture of need and use of services.

Existing procedures

For investigation of abnormal uterine bleeding, the most commonly used diagnostic procedures are TVS, EMB, dilatation and curettage (D&C), and diagnostic hysteroscopy.

Hysteroscopy (with pathology findings) has been most frequently used as the 'gold standard'. If it is performed, hysterectomy also provides a definitive diagnosis.

While there are presently no clinical practice guidelines in place for the investigation of abnormal uterine bleeding, diagnostic procedures in Australia usually involve blind endometrial biopsy and/or hysteroscopy; or TVS followed by EMB/hysteroscopy.

Comparator

As SIS is to be used in conjunction with TVS as a second-line diagnostic procedure, it is appropriate to compare TVS plus SIS with TVS alone.

Marketing status of the device

The equipment used for SIS has been listed by the Therapeutic Goods Administration. There are many brands made by different manufacturers available in the Australian market, but no particular brand is nominated in the application.

Current reimbursement arrangement

Currently there is no specific Medicare Benefits Schedule item number for SIS procedures.

Approach to assessment

MSAC reviewed the available literature on the use of SIS to investigate abnormal uterine bleeding and convened a supporting committee to review the evidence and provide expert advice.

Review of literature

DialogWeb was used to sweep medical and health related databases (up to 40, including Medline, Healthstar and EMBASE). The search covered the period from the establishment of each individual database to June 1998. The following search terms were used: sonohysterography, SIS, sonohysterosalpingography; and hysteroscopy, uterine bleeding, infertility, abortion, randomized controlled trial, systematic review, meta analysis.

Fifty-four publications were identified and 38 full publications were retrieved; 14 studies are included in this report.

Studies were included if they met the following criteria:

- patients enrolled in the study suffered from abnormal uterine bleeding;
- SIS results were confirmed by hysteroscopy/hysterectomy with or without pathology reports; and
- TVS was compared with TVS+SIS, or TVS was compared with SIS.

Studies were excluded if they were a general review of the SIS technique or:

- SIS was used in patients with infertility or abortion, or under tamoxifen treatment; and
- SIS findings were not confirmed by hysteroscopy or hysterectomy.

The evidence presented in the selected studies was assessed and classified according to the National Health and Medical Research Council (NHMRC) revised hierarchy of evidence, which is shown in Table 1.

Table 1 Designation of levels of evidence

I	Evidence obtained from a systematic review of all relevant randomised controlled trials.
II	Evidence obtained from at least one properly designed randomised controlled trial.
III-1	Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).
III-2	Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case-control studies or interrupted time-series with control group.
III-3	Evidence obtained from comparative studies with historical control, two or more single-arm studies or interrupted time series without a parallel control group.
IV	Evidence obtained from case series, either post-test or pre-test and post-test.

Source: NHMRC. [3]

The design and quality of the selected studies are shown in Table 2.

Table 2 Characteristics of the studies

Level of evidence	Author	Study design	Confirmation (gold standard)	Subjects
Level II	Saidi et al 1997[4]	RCT ('head-to-head'): patients underwent either TVS or SIS, Open design	Hysteroscopy /EMB + pathology	*n*=68 Mean age>40 (range not stated)
Level III-2	Dubinsky et al 1995[5]	Patients screened with EMB and TVS, then SIS performed on 81/148 with endometrium >5 mm. Open design	Hysteroscopy/ hysterectomy + pathology	*n*=81 Mean age=56 (42–84)
Level III-2	De Crespigny et al 1997[6]	Patients screened with TVS, SIS was performed on 55 patients. Open design	Hysteroscopy	*n*=55 (60 enrolled) Abnormal uterine bleeding Mean age not stated (6 postmenopausal)
Level III-2	Parsons et al 1996[7]	SIS (no details given)	Hysterectomy + pathology	*n*=53 Scheduled for hysterectomy due to abnormal uterine bleeding Mean age and range not stated
Level III-2	Lev-Toaff et al[8]	Patients screened with TVS; SIS was performed on 28 patients with abnormal TVS. Open design	Hysteroscopy + pathology	*n*=28 Abnormal uterine bleeding (premenopausal) Mean age=41.8±7.01 (29–55)
Level III-2	Goldstein et al 1997[9]	Patients screened with TVS, followed by SIS Open design	D&C, hysteroscopy, or EMB + pathology	*n*=153 (433 enrolled) Mean age not stated (>39)
Level III-2	Cicinelli et al 1995[10]	Patients screened with TVS, then transabdominal SIS Investigator blind	Hysteroscopy and hysterectomy	*n*=52 Premenopausal bleeding (35) and multiple myomas(17), scheduled for hysterectomy Mean age=not stated (40–51)
Level III-2	Gaucherand et al 1995[11]	Patients screened with TVS, followed by SIS Open design	Hysteroscopy (82/104) + pathology	*n*=104 (82 had hysteroscopy) Mean age not stated
Level III-2	Laughhead and Stones 1997[12]	Patients screened with TVS, followed by SIS if endometrium >5 mm Open design	D&C, EMB or hysteroscopy + pathology	*n*=124 (114 SIS) Mean age=48 (36–70)
Level III-2	Turner et al 1995[13]	Patients screened with TVS, followed by SIS Open design	Hysteroscopy and operative procedure + pathology	*n*=30 (23 SIS) Mean age=40 (29-64)

Table 2 (contd)

Level of evidence	Author	Study design	Confirmation (gold standard)	Subjects
Level III-2	Bernard et al 1997[14]	Patients underwent SIS Open design	Hysteroscopy and operative procedure + pathology	*n*=162 109 premenopausal: mean age=41.1±6.8 (21–54) 53 postmenopausal: mean age=57.8±8.9 (42–81)
Level III-2	Cohen et al 1994[15]	Patients underwent TVS, followed by SIS Open design	Hysteroscopy + pathology	*n*=15 Mean age not stated (52–73)
Level III-2	Cicinelli et al 1994[16]	Patients screened by TVS, then transabdominal and transvaginal SIS Investigator blind	Hysteroscopy and hysterectomy + pathology	*n*=50 (43 SIS) premenopausal Mean age not stated (39–49)
Level III-2	Wolman et al 1996[17]	Patients underwent TVS, followed by SIS Investigator performing hysteroscopy was blinded	Hysteroscopy	*n*=50 (47 SIS) Mean age and range not stated

Study design

In most studies (11 of 14) TVS was used as a first-line screening diagnostic procedure for patients with abnormal uterine bleeding. Those patients with abnormal but inconclusive TVS findings were further examined by SIS, and the final diagnosis was confirmed by hysteroscopy and/or hysterectomy with or without pathology confirmation. In three studies, investigators performing SIS were blinded from the results of other procedures.[10,16,17]

There was only one randomised controlled trial (RCT), which was a direct comparison of TVS and SIS ('head-to-head').[4] The randomisation was not conducted using a secured method, because 68 eligible patients were numbered consecutively and assigned to either the TVS (even number) or SIS (odd number) groups. The diagnosis was confirmed by hysteroscopy, hysterectomy, or D&C. Results were analysed on an 'intention-to-treat' basis. The trial was unblinded in design (blinding would be difficult because information other than images is required for ultrasonologists to conclude ultrasound findings).

'Gold standard' for diagnosis of uterine bleeding

Hysteroscopy and hysterectomy are both 'gold standards' for diagnosis of uterine bleeding. However, the two procedures are quite different in terms of invasiveness, accuracy, and appropriateness for different circumstances. Hysteroscopy was the most frequently used 'gold standard' in the studies, though hysterectomy was sometimes used. Pathology results were available in 11 of 14 studies.

Representativeness

There are no Australian clinical practice guidelines for the diagnosis of uterine bleeding, but the supporting committee provided information suggesting that the diagnostic workup for abnormal uterine bleeding involves initial TVS investigation, followed by EMB or hysteroscopy; or, alternatively, blind EMB and/or hysteroscopy. In view of this, all studies

included in this review except the RCT[4] were considered to be representative of patient groups for whom funding is sought under Medicare.

Bias

Blinding was applied in only three studies:[10,16,17] either the investigators were blinded from the results of all other procedures,[10,16] or the investigators performing hysteroscopy were blinded from the results of TVS and SIS[17].

Intention-to-treat analysis

Eight of the14 studies failed to report results on all patients who underwent SIS.[6,9–14,16]

Expert advice

A supporting committee including clinicians with expertise in obstetrics and gynaecology was convened to assess the evidence available on this procedure. In selecting members for supporting committees, MSAC's practice is to approach the appropriate medical colleges, specialist societies, and associations for nominees. Membership of the supporting committee is shown in Appendix B.

Results of assessment

Is it safe?

Symptoms such as discomfort, minor cramping, and mild menstrual-like pain have been reported during the SIS procedure; they are associated with instillation of saline into the uterine cavity. There is potential risk of infection but, among six studies in which adverse events were reported (out of the total of 14 studies), endometritis was seen in only one study (2.5%). There were no adverse events seen in three of these six studies.[11,13,14] The reported adverse events are summarised in Table 7.

Table 3 Adverse events

		SIS	
Study	**Adverse events**	***r/n***	**%**
Dubinsky et al[5]	Endometritis	2/81	2.5
Laughhead and Stones[12]	Mild cramping	38/114	33.3
Cicinelli et al[16]	Severe pain	5/43	11.6
	Parasympathetic reaction	4/43	9

r = number of reports; *n* = number of patients; SIS = saline infusion sonohysterography

Is it effective?

In the 14 studies selected, outcomes were assessed against the following criteria:

- sensitivity and specificity
- positive and negative predictive values
- clinical impact

Sensitivity and specificity

In seven of the studies, sensitivity and specificity were not reported but the diagnosis was assessed using endpoints such as thickened endometrium, polyp, or myomas, and the results were compared with the results of hysteroscopy or hysterectomy as the 'gold standard'.[5,6,8,9,12,13,15] There was good agreement between the findings of TVS+SIS and the results confirmed by hysteroscopy and/or hysterectomy. Further details are shown in Appendix C.

In a further six studies, the findings of TVS and TVS+SIS were calculated against the 'gold standard' and presented as sensitivities and specificities. There was excellent agreement between the findings of TVS+SIS and the results confirmed by hysteroscopy and/or hysterectomy.[7,10,11,14,16,17] In four of these six studies, the sensitivity and specificity were reported on different lesions (polyps, submucosal myomas, endometrium atrophy or thickening, and carcinoma).[10,11,14,16] The sensitivity and specificity of TVS+SIS in diagnosis of different uterine abnormalities and the 95% confidence intervals (95% CI) are presented in Table 3. Further details are shown in Appendix C.

It is generally accepted that the usual cause of abnormal uterine bleeding is dysfunctional bleeding (up to 80% of patients) and the incidence of endometrial carcinoma is relatively

low. This is reflected in the studies retrieved, in which 11 cases of carcinoma were reported.[5,14,15] Endometrial carcinoma often results in abnormal uterine bleeding and thickened endometrium; SIS can detect the lesion and provide guidance for further investigations, for example, hysteroscopy and/or hysterectomy.[18]

In the study of Bernard, three cancer cases were misdiagnosed by SIS as polyp, hypertrophy and submucous myomas.[14] However, as all these findings warranted further exploration, the possibility of a false negative diagnosis was limited.

The remaining study was the only RCT and was a direct ('head-to-head') comparison of SIS and TVS.[4] As with the other studies, the diagnosis was confirmed by hysteroscopy or biopsy. The sensitivity and specificity determined from this trial for SIS and TVS are shown in Table 4.

Predictive values

The positive predictive value (PPV) and negative predictive value (NPV) for SIS and TVP were reported in the RCT[4] and are shown in Table 4.

The PPV and NPV were also reported in three of the comparative studies[10,11,16] and are shown in Table 5. SIS with TVS gave similar or slightly better PPVs and NPVs than TVS alone.

The NPV of SIS was significantly lower in the RCT (Table 4) than in the comparative studies (Table 5). Lack of detailed data prevents a recalculation. However, the RCT, which is a direct comparison of TVS and SIS, does not reflect the expected use of SIS in Australian clinical practice.

Table 4 Sensitivity and specificity of TVS+SIS from comparative studies (level III-2 evidence)

Uterine lesions	Sensitivity (95% CI)				Specificity (95% CI)			
	Lower estimates (%)		Upper estimates (%)		Lower estimates (%)		Upper estimates (%)	
Polyps	86	(76–96)	96	(92–100)	90	(84–96)	100	
Submucosal myomas	89.6	(85–94)	100		95	(92–98)	100	
Atrophy	80	(71–87)	98.9	(97–100)	76.4	(70–83)	100	
Cancer								
Ref 6 (*n*=5)	100							
Ref 1 (*n*=5)	40				100 (2 cases)		100	
Ref4 (*n*=1)	0							

CI = confidence interval
Sources: Cicinelli et al,[16] Cicinelli et al,[10] Gaucherand et al,[11] Wolman et al,[17] Parsons et al,[7] Bernard et al.[14]

Table 5 Sensitivity and specificity of TVS or SIS from an RCT (level II evidence)

Procedure	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	NPV (%) (95% CI)	PPV (%) (95% CI)
SIS	90.9 (78.9–100)	83.3 (62.2–100)	16.7 (–4–37.8)	90.9 (78.9–100)
TVS	95.7 (87.4–100)	63.6 (35.2–92)	12.5 (–7–32)	84.6 (69.8–99.4)
Diagnostic hysteroscopy	82.2 (71–93.4)	65.2 (45.7–84.7)	45.5 (16.1–74.9)	78.3 (61.5–95.1)

TVS = transvaginal ultrasound; SIS = saline infusion sonohysterography; PPV = positive predictive value; NPV = negative predictive value
Source: Saidi. [4]

Table 6 Predictive values from comparative studies (level III-2 evidence)

Study	PPV (%)		NPV (%)	
	TVS+SIS	TVS	TVS+SIS	TVS
Cicinelli et al[10]	100	90	100	98
Gaucherand et al[11]	91	88	99	97
Cicinelli et al[16]	100	100	91.2	79.5

PPV = positive predictive value; NPV = negative predictive value; TVS = transvaginal ultrasound; SIS = saline infusion sonohysterography

Accuracy of TVS+SIS compared with TVS alone

When compared with TVS, TVS+SIS increased the sensitivity in the detection of a number of uterine cavity lesions, polyps, submucosal myomas and endometrial atrophy.[10,11,16] However, SIS gave little improvement in specificity. Details of comparative sensitivity and specificity are shown in Table 6.

Table 7 Accuracy of TVS+SIS and SIS alone

	Sensitivity (%)		Specificity (%)		Difference (95%CI, *P* value)	
Uterine lesions	**TVS+SIS**	**TVS**	**TVS+SIS**	**TVS**	**Sens**	**Spec**
Polyps						
Gaucherand et al[11]	96	71	90	88	25 (18.1–31.8, *P*<0.001)	2 (–4.1–8.1, ns)
Cicinelli et al[16]	75[a]	33.3	100	100	41.7 (33.1–50.8, *P*<0.001)	0
	58.3[b]	33.3	100	100	25 (15.5–34.4, *P*<0.001)	0
Submucosal myomas						
Cicinelli et al[10]	100	90	100	98	10 (5.8–14.1, *P*<0.001)	2 (–4.1–8.1, ns)
Gaucherand et al[11]	100	100	100	94.5	0 (1.9–8, *P*<0.01)	5.5
Atrophy						
Gaucherand et al[11]	80	50	100	98	30 (21.1–38.8, *P*<0.001)	2 (–4.1–8.1, ns)
Nonspecified uterine abnormality						
Saidi et al[4]	90[c]	95	83[c]	65	–5 (–10–0.1, ns)	18 (9.5-26.4,*P*<0.001)

ns = not significant (*P*>0.05); TVS = transvaginal ultrasound; SIS = saline infusion
[a] Transabdominal SIS
[b] Transvaginal SIS
[c] SIS only ('head to head' trial)

Influence on clinical decision making/health outcomes

De Crespigny reported limited data from 55 patients recommended by their gynaecologists for hysteroscopy due to abnormal uterine bleeding.[6] Eleven patients (20%) avoided this procedure following a normal SIS. The difference was statistically significant (*P*<0.001).

The results of the RCT suggested that SIS investigation reduced the requirement for diagnostic hysteroscopy from 76.5% (26/34) to 64.7% (22/34), compared with TVS used alone. However, the difference was not statistically significant (*P*=0.13).

No data are available to estimate the implications of SIS on health outcomes.

Economic considerations

There are insufficient data available to allow a reliable cost-effectiveness analysis. Incremental costs and incremental cost-effectiveness ratios have been calculated using assumptions derived from the study of de Crespigny, but the results should be interpreted with caution because of the bias inherited from this study.[6] The need for economic modelling has not been established.

Clinical benefits

The studies show that the use of SIS will benefit clinical decision making, with up to 20% of patients avoiding diagnostic hysteroscopy.[6] Hysteroscopy is a more invasive procedure, and is associated with significant financial cost, as well as physical discomfort.

Costs

Weighted average costs were estimated from the Medicare usage of diagnostic hysteroscopy (items 35626, 35627 and 35630) and TVS (items 55042 and 55043) for the 1996–97 financial year (information obtained from Financing and Analysis Branch, Health Benefits Division, Department of Health and Aged Care). The exact usage of TVS and hysteroscopy for abnormal uterine bleeding is not known because the data collected on utilisation of Medicare services do not capture the indication used under the item.

Weighted average health care costs

The weighted average costs for diagnostic hysteroscopy, TVS and EMB are shown in Table 8.

Table 8 Weighted average costs for diagnostic hysteroscopy, TVS and EMB

Procedure	Calculated cost ($)
Diagnostic hysteroscopy[a]	
Public patient	1,111.80
Private patient	934.90
TVS	92.47
EMB	130.59
SIS[b]	279.22

[a] Takes into consideration the anaesthetic and one-day hospital stay
[b] Includes fees for both TVS and the subsequent SIS; takes about 60 minutes to perform
TVS = transvaginal ultrasound; EMB = endometrial biopsy; SIS = saline infusion sonohysterography

Cost of adverse events

Adverse events reported requiring medical treatment were not common, and prophylactic antibiotics were not routinely used. For simplicity, the costs associated with adverse events were therefore not considered.

Other costs

Costs incurred by individual patients, costs to the hospital budget and other health care costs are comparable in patients receiving TVS and patients receiving TVS+SIS; they are therefore excluded in this review to simplify the calculation.

Incremental costs

It is not known how many women underwent diagnostic hysteroscopy as public patients and how many as private patients. Table 9 shows the incremental costs for public and private patients. The cost differences are modelled on a cohort of 100 patients undergoing TVS or TVS+SIS. The incremental costs of SIS are largely offset by the reduced use of hysteroscopy, which is an inpatient procedure and is associated with higher costs. The cost-effectiveness ratios are sensitive to the proportion of patients in whom hysteroscopy could be avoided.

Table 9 Incremental costs of SIS

	TVS+hysteroscopy *n*=100	TVS+SIS+hysteroscopy *n*=100	Incremental cost of SIS
Public patients			
Cost of TVS	$92.47×100=$9247	$279.22×100=$27,922	$18,675
Cost of hysteroscopy	$1,111.8×100=$111,179	$1,111.8×80=$88,943	–$22,236
Total	$120,426	$116,865	–$3561
Private patients			
Cost of TVS±SIS	$92.47×100=$9247	$279.22×100=$27,922	$18,675
Cost of hysteroscopy	$934.9×100=$93,490	$934.9×80=$74,792	–$18,698
Total	$102,737	$102,714	–$23

TVS = transvaginal ultrasound; SIS = saline infusion; *n* = number of patients

Data on Medicare usage in the 1996–97 financial year shows that 2600 EMB services (MBS items 35620 and 35622) have been used in conjunction with TVS (MBS items 55042 and 55043), at an estimated cost of $339,542 per year. However, there were no clinical data on the proportion of patients in whom EMB was avoided following SIS. Therefore, possible savings on EMB could not be calculated.

Incremental cost-effectiveness ratios

- For public patients
  - incremental cost of SIS per 100 patients: –$3561 (saving)
  - incremental benefits (hysteroscopy avoided): 20%
  - SIS is dominant in incremental cost-effectiveness ratio, with a cost saving of $3561 per100 patients.

- For private patients
  - incremental cost of SIS per 100 patients: –$23 (saving)
  - incremental benefits (hysteroscopy avoided): 20%
  - SIS is cost neutral to TVS, with a cost saving of $23 per 100 patients.

Sensitivity analysis

The sensitivity analysis has been conducted using the lower and the higher estimate of the 95% CI (9.4%, 30.6%) of the incremental benefits, that is, the proportion of patients who avoided hysteroscopy.

- For public patients
  If 9.4% of patients avoided hysteroscopy:
  - incremental cost of SIS per 100 patients: $8224
  - incremental cost-effectiveness ratio: $875/extra hysteroscopy avoided

  If 30.6% of patients avoided hysteroscopy
  - incremental cost of SIS per 100 patients: –$15,346 (saving)
  - SIS is dominant in incremental cost-effectiveness ratio, with a cost saving of $15,346/100 patients.

- For private patients
  If 9.4% of patients avoided hysteroscopy:
  - incremental cost of SIS per 100 patients: $9887
  - incremental cost-effectiveness ratio: $1052/extra hysteroscopy avoided

  If 30.6% of patients avoided hysteroscopy:
  - incremental cost of SIS per 100 patients: –$9932 (saving)
  - SIS is dominant in incremental cost-effectiveness ratio, with a cost saving of $9932/100 patients.

Other considerations

SIS has been used for broader indications than abnormal uterine bleeding (for example, monitoring during tamoxifen therapy, investigation of infertility). Additional evaluation will be required to ascertain the effectiveness of SIS for these indications.

There is no proposed restriction to service providers.

Conclusions

Safety

SIS is a safe procedure with a low incidence of minor complications and no major complications.

Effectiveness

The data examined in this report suggest that SIS+TVS has a higher sensitivity than TVS alone in detection of uterine cavity abnormalities, and has a similar specificity. The use of SIS benefits clinical decision making, because a proportion of patients will avoid diagnostic hysteroscopy, which is a more invasive procedure and is associated with physical discomfort and increased financial cost.

Cost-effectiveness

Assuming that a reduction in hysteroscopies is of clinical benefit, and using the finding of de Crespigny that, following SIS, 20% of patients avoid a hysteroscopy, then SIS is associated with a cost saving of between $23 per 100 patients to $3561 per 100 patients.[6] Sensitivity analysis indicates that the incremental cost-effectiveness ratio could be up to $1052 per extra hysteroscopy avoided.

Other considerations

The appropriate clinical place for SIS is as a second-line diagnostic procedure for abnormal uterine bleeding, if TVS findings are inconclusive.

There appears to be a place for clinical practice guidelines for the management of abnormal uterine bleeding. They should cover an initial investigational TVS, followed by SIS where indicated, with further clinical management (hysteroscopy, surgery or conservative management), as necessary. This concept is supported by current international clinical practice as revealed in the literature.

SIS may be most useful in diagnosis of thickened endometrium and endometrial polyps, and the level of sensitivity and specificity may vary in different clinical conditions. The introduction of SIS is expected to decrease the use of hysteroscopy and blind endometrial biopsy.

The supporting committee concluded that SIS is a safe procedure, noting that in Australia prophylactic antibiotics are not routinely used following this procedure.

Recommendation

MSAC recommended that on the strength of evidence pertaining to saline infusion sonohysterography, public funding should be supported for this procedure as a second-line diagnostic procedure for abnormal uterine bleeding, when findings from transvaginal ultrasound are inconclusive.

? The Minister for Health and Aged Care accepted this recommendation on 11 May 1999 ?

Appendix A MSAC terms of reference and membership

The terms of reference of the Medicare Services Advisory Committee are to advise the Commonwealth Minister for Health and Aged Care on:

- the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost effectiveness and under what circumstances public funding should be supported;
- which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost effectiveness; and
- references related either to new and/or existing medical technologies and procedures.

The membership of the Medicare Services Advisory Committee comprises a mix of clinical expertise covering pathology, nuclear medicine, surgery, specialist medicine and general practice, plus clinical epidemiology and clinical trials, health economics, consumers, and health administration and planning:

Member	**Expertise**
Professor David Weedon (Chair)	pathology
Ms Hilda Bastian	consumer health issues
Dr Ross Blair	vascular surgery (New Zealand)
Mr Stephen Blamey	general surgery specialising in colorectal endoscopy and laparoscopic surgery
Dr Paul Hemming	general practice
Dr Terri Jackson	health economics
Professor Brendon Kearney	health administration and planning
Dr Richard King	gastroenterology
Dr Michael Kitchener	nuclear medicine
Professor Peter Phelan	paediatrics
Dr David Robinson	plastic surgery
Ms Penny Rogers	Assistant Secretary of the Diagnostics and Technology Branch of the Commonwealth Department of Health and Aged Care
Associate Professor John Simes	clinical epidemiology and clinical trials
Dr Bryant Stokes	neurological surgery, representing the Australian Health Ministers' Advisory Council (since 1/1/99)
Dr Doris Zonta	population health, representing the Australian Health Ministers' Advisory Council (until 31/12/99)

Appendix B Supporting committee

MSAC application 1007
Saline infusion sonohysterography

Dr Michael Kitchener (Chair) MBBS, FRACP Senior Visiting Medical Specialist, Queen Elizabeth Hospital, Adelaide; Director, Nuclear Medicine, Dr Jones and Partners, St Andrews Hospital, Adelaide	member of MSAC
Professor David Ellwood FRACOG, MA, DPhil, DDU Professor of Obstetrics and Gynaecology, Canberra Clinical School, University of Sydney; Medical Director, Women's and Children's Health, The Canberra Hospital	co-opted member
Assoc. Professor Lachlan de Crespigny MD, BS, FRCOG, FRACOG, DDU, COGUS Head of Ultrasound Department, Royal Women's Hospital, Melbourne; Department of Obstetrics and Gynaecology, University of Melbourne	nominated by the Australian Association of Obstetrical and Gynaecological Ultrasonologists
Ms Mari-Ann Scott BEc Hon, MPhil Senior Policy Analyst, Acute Health Division, Department of Human Services, Victoria	health economist

Appendix C Results of TVS and TVS+SIS in diagnosis of abnormal uterine bleeding

Study	Agreement with hysteroscopy/hysterectomy				Sensitivity and specificity
Dubinsky et al 1995[5]		TVS+SIS	EMB	Hysteroscopy /hysterectomy	Not reported
n=81	Endometrial mass	45	4	45	
	Endometrial cancer	5	2	5	
	Normal	36	36	36	
de Crespigny et al 1997[6]		TVS+SIS	TVS	Hysteroscopy	Not reported
n=55	Polyp	12	not certain	10	
	Fibroid	7	7	—	
	Normal	7	7	—	
Lev-Toaff et al 1996[8]		TVS+SIS		Hysteroscopy	Not reported
n=28	TVS abnormal endometrial (*n* =14):				
	Polyps	9		8	
	Submucous Fibroid	3		2	
	Endometrial>8 mm	2		2	
	TVS fibroid (*n* =14):				
	Fibroid	14		14	
Goldstein et al 1997[9]		TVS+SIS		Hysteroscopy	Not reported
	Polypoid	58		58	
	Submucous myomas	22		22	
n=153	Endometrial >3 mm	10		10	
	Endometrial >5 mm	61			
	Inadequate vision	2			
Cicinelli et al 1995[10]		TVS	TVS+SIS (transabdominal)	Hysteroscopy /hysterectomy	TVS / TVS +SIS / Hysteroscopy
	Submucous myomas	9	10	10	Sens 90% / 100% / 100%
n=52	Polyp	0	1	1	Spec 98% / 100% / 100%
	Opt time (min)	7.4±1 (*P*<0.001)	13.6±1.3	10.6±1.1	The estimation was made on the total of 52 patients, assuming endometrial polyps to be 'normal'.
	(No mention of the rest of 41 patients, normal?)				
Gaucherand et al 1995[11]	No details available				TVS / TVS +SIS / Hysteroscopy
n=104					Polyp: Sens 71% / 96% / 28; Spec 88% / 90%
					Myomata: Sens 100% / 100% / 19; Spec 94.5% / 100%
					Atrophy: Sens 50% / 80% / 11; Spec 98% / 100%
					(no mention of the rest of 24 patients)
Laughhead & Stones 1997[12] *n*=114		TVS+SIS	TVS	EMB /hysteroscopy	Not reported
	Intramural myomas	48	48	48	
	Submucous myomas	8	0	8	
	Polyp	18	0	18	
	Endometrial >5 mm (*n* =46)	46	46	2 polyp	
	(no detailed data presented)				
Turner et al 1995[13]		TVS+SIS	TVS	Hysteroscopy	Not reported
	Submucous myomas	10	10	9	
	Polyp	8	8	9	
n=23	(no mention of the rest of 5 patients)				

Study	Agreement with hysteroscopy/hysterectomy			Sensitivity and specificity			
Bernard et al19971[4] *n*=162		SIS	Pathology		SIS		
	Atrophy/normal	13	17	Polyp			
	Hypertrophy	18	16	Sens	87.8%		
	Polyp	29	33	Spec	90.7%		
	Submucous myomas	26	29	Submucosal myomata			
	Intramural myomas	6	6	Sens	89.6%		
	Adenomyosis	1	1	Spec	95%		
	Cancer	2	5	Atrophy			
	(3 cancer diagnosed by pathology were misdiagnosed by SIS as polyp, hypertrophy, and submucous myomas)			Sens	98.9%		
				Spec	76.4%		
				Cancer			
				Sens	40%%		
				Spec	100%		
Wolman et al 1996[17] *n*=47		TVS+SIS	Hysteroscopy		TVS+SIS		
	Normal	10	10	Sensitivity	86%		
	One polyp	25	20	Specificity	100%		
	>One polyp	0	3				
	Fibroid	12	14				
Cohen et al 1994[15] *n*=15		TVS+SIS	Hysteroscopy	Not reported			
	Polyp	7	8				
	Hyperplasia	4 irregular lining	3				
	Atrophy	0	3				
	Carcinoma	0	1				
	Normal	4					
Cicinelli et al 1994[16] *n* =43		TVS+SIS (transabdominal)	TVS	Hysteroscopy /pathology		TVS[a]	TVS +SIS[b]	TVS +SIS[c]
	Cervical polyp	0(5)	0	5	Polyps			
	Endometrial polyp	7(5)	4	8	Sens	33.3%	75%	58.3%
	Myomas	5(5)	6	5	Spec	100%	100%	100%
	Opt time(min)	15.7±2.1 (14.2±2)	8.0±1.7	11.2±1.7	Combined SISs (abd+vag)			
	(no mention of rest of 29 patients)				Sens	91.7%		
					Spec	100%		
					The estimation was made on the total of 43 patients, assuming myomas to be 'normal'.			
					[[a]=abdominal; [b]=transvaginal; [c]=endouterine.]			
Parsons et al 1996[7] *n*=53	No details available			SIS correctly diagnosed 95% of lesions, confirmed by hysterectomy and pathology (no details given).			
Saidi et al 1997[4] *n* =68		SIS	Hysteroscopy	Pathology		TVS	SIS	hysteroscopy
	Normal	12	12	12	Sens	95%	90%	78%
	Abnormal endometrial	4	5	4	Spec	65%	83%	54%
	Intrauterine cavity structure	15	13	16				
	Uterine septum	2	1	1				
	Inconclusive	1	3	0				
		TVS	Hysteroscopy	Pathology				
	Normal	8	11	11				
	Abnormal endometrial	9	6	2				
	Intrauterine Cavity structure	16	14	20				
	Uterine septum	0	0	0				
	Inconclusive	1	3	0				
	Blood clot			1				

TVS = transvaginal ultrasound; EMB = endometrial biopsy; SIS = saline infusion sonohysterography

Abbreviations

CI	confidence interval
D&C	dilatation and curettage
EMB	endometrial biopsy
MBS	Medicare Benefits Scheme
MSAC	Medicare Services Advisory Committee
NHMRC	National Health and Medical Research Council
NPV	negative predictive value
PPV	positive predictive value
RCT	randomised controlled trial
SIS	saline infusion sonohysterography
TVS	transvaginal ultrasound

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