

Impact of Guglielmi detachable coils on outcomes of patients with intracranial aneurysms treated by a multidisciplinary team at a single institution

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Object. The goal of this study was to investigate the impact of the introduction of the Guglielmi detachable coil (GDC) therapeutic option on the overall management outcome of intracranial aneurysms. The authors accomplished this by assessing patient morbidity and mortality, inflation-adjusted hospital charges, lengths of stay in the hospital and the intensive care unit (ICU), and treatment efficacy.

Methods. The authors conducted a retrospective analysis of consecutive cases of intracranial intradural aneurysms managed by a single multidisciplinary neurovascular team at a tertiary care, academic referral center during the 24 months preceding the introduction of the GDC procedure (Group I or pre-GDC era, 77 patients) and during the first 24 months after its introduction (Group II or GDC era, 99 patients).

Treatment with GDCs was considered for cases of higher clinical grade or poor surgical risk, or in response to patient preference (27 [27%] of 99 patients in Group II). Host and lesion parameters in our cohort were validated against outcome parameters by using univariate and multivariate analyses. The pre-GDC and GDC subgroups of patients were comparable for major disease severity parameters (patient age, lesion location, clinical grade, and hemorrhage severity). There was no significant difference in clinical outcome at 6 months, infarcts on computerized tomography scanning, or aneurysm obliteration rates before and after introduction of GDC treatment. Decreasing trends in duration of hospital and ICU stay and in inflation-adjusted hospital charges occurred well before and thus were unrelated to the introduction of the GDC therapeutic option.

Conclusions. The results of this study do not demonstrate any significant impact of integration of the GDC modality on clinical outcome, mortality, morbidity, or effectiveness of treatment. Ongoing improvements in hospital charges and length of hospital stay appeared unrelated to the introduction of the GDC option.

KEY WORDS • cerebral aneurysm • Guglielmi detachable coil • outcome • hospital charge

THE goal of treatment of intracranial aneurysms is to exclude the lesion from the cerebral circulation and to prevent subsequent hemorrhage. Although this can be achieved by microsurgical clipping of the aneurysm neck in most cases, the introduction of GDCs has provided an alternative option to treat many lesions.^{32–35} This approach was designed to offer a potentially less morbid endovascular approach via transfemoral superselective catheterization of an aneurysm, followed by endosaccular occlusion with microcoils. Such a technique is particularly attractive in circumstances in which open surgery is associated with relatively increased risk. The GDC procedure allows early therapeutic intervention, often at

the same setting as the initial diagnostic angiographic study, making it particularly appealing in patients with high clinical grades, who may be medically or neurologically unstable.^{5,6,12,29,36,59,61,81,82,90,92,105} It avoids brain retraction associated with open surgery, which may be harmful in the swollen brain after acute hemorrhage. It also has been suggested that this method may be safer than microsurgical clipping of selected aneurysms in locations where surgery may be more difficult or risky (such as aneurysms located in the posterior circulation or giant aneurysms),^{19,27,55,79,84} in older patients, and in patients with comorbid medical conditions.^{3,6,10,12,24,40,57,60,72,92} With recent advances in microcatheters, aneurysms located at practically any site can be reached and potentially obliterated, particularly aneurysms with narrower neck configurations and smaller sizes,²⁰ as long as the aneurysm does not incorporate the parent artery or its branches.

There have been several concerns about the GDC pro-

Abbreviations used in this paper: CT = computerized tomography; GDC = Guglielmi detachable coil; GOS = Glasgow Outcome Scale; ICU = intensive care unit; LOS = length of stay; SAH = subarachnoid hemorrhage; US = United States.

cedure, including its failure to obliterate certain aneurysms after it is used or attempted, potential recanalization of the aneurysm from coil compaction, and regrowth of the aneurysm after endosaccular occlusion.^{62,69,81,101} There has also been speculation that potential complications of the GDC procedure or patient illness may offset any advantage of endosaccular coil embolization in some cases.^{1,68,77} The safety and short-term efficacy of GDC embolization in ruptured and unruptured aneurysms have been reported extensively in several selected uncontrolled series,^{6,9,12,19,27,55,57,65,66,78,84,92,101} and there are reports addressing the issues of failed GDC treatment followed by surgical therapy, failed aneurysm clipping followed by GDC therapy, and planned combined therapies for complex lesions.^{7,31,37,48,100} However, the impact of this treatment modality on the overall multidisciplinary management outcome of intracranial aneurysms has not yet been investigated.

A number of host and lesion factors have been correlated with management outcome of intracranial aneurysms by using a paradigm of microsurgical clipping and early treatment intervention after SAH. These include the patient's clinical grade (neurological and medical sequelae of prior hemorrhage),⁴³ advanced age,^{2,52,58,97,98} and preexisting medical illness.¹⁰⁶ The extent of the initial hemorrhage (often reflected in the patient's early clinical condition and subsequent ischemic damage from vasospasm) as well as aneurysm location (anterior or posterior circulation), size (small, large, or giant), and multiplicity of aneurysms have also been correlated with treatment outcome.^{22,39,45,52,53,73,74,85,89,94–96,102} Few researchers have published evaluations of the influence of these variables in patient cohorts managed by surgical and endovascular (GDC) therapeutic options.^{12,60}

In several studies the economic impact of treatment of ruptured and unruptured intracranial aneurysms has been considered in terms of cost, hospital LOS, and other resource utilization.^{17,18,26,42,44,45,50,54,75,97,99,108,110} Although endovascular therapy may reduce hospital and ICU LOS compared with those associated with microsurgical treatment, cases treated by the two modalities have not been matched concurrently. In no study has the impact of the introduction of the GDC treatment option on the overall cost of aneurysm care been examined.

It has been suggested that the GDC treatment option theoretically may allow selection of patients with greater surgical risk for a less invasive and potentially less morbid therapeutic alternative. Such selection of high-risk patients might improve the overall management outcome of all cases.^{5,6,12,29,50,55,57,60,92,101,105} It has also been postulated that such integration of GDC treatment would maintain treatment efficacy (aneurysm obliteration) while decreasing the overall cost of care. In this study we examined the impact of the introduction of the GDC treatment option on the outcomes of multidisciplinary management of intracranial aneurysms treated at a single institution. We compared outcomes of multidisciplinary management of all intracranial intradural aneurysms in two cohorts of consecutive cases, treated just before and after the introduction of the GDC treatment option. This procedure was introduced by our team after approval of the GDC by the United States Food and Drug Administration and following the approved training and certification of our team

members. The GDC treatment option was selectively considered and offered to patients in whom we anticipated increased surgical risk (patients with high clinical grades, older patients, and patients harboring posterior circulation aneurysms)^{12,34,57} and to patients who refused traditional microsurgical options. We hypothesized that the introduction of the GDC option was associated with improved overall management outcome of intracranial aneurysms, as assessed by rates of patient morbidity and mortality, inflation-adjusted hospital charges, LOS in the hospital and the ICU, and treatment efficacy.

Clinical Material and Methods

Patient Population

We conducted a retrospective review and analysis of consecutive cases of intracranial intradural aneurysms managed by the neurovascular surgery program team at Yale–New Haven Hospital (a tertiary care center) during the 24 months preceding the introduction of the GDC procedure (Group I or pre-GDC era) and during the first 24 months following its introduction (Group II or GDC era). Extradural aneurysms, including petrous, cavernous, and dissecting aneurysms, were excluded. In patients with multiple aneurysms, each hospitalization for aneurysm treatment was considered as a separate encounter, and LOS and hospital charges were assessed for each encounter. If a patient had multiple hospitalizations for the same aneurysm, the LOS and hospital charges were assessed cumulatively. Procedure-related outcome parameters (aneurysm obliteration, morbidity and mortality, and postprocedure brain infarcts) were assessed individually whenever possible for each treatment rendered, and cumulatively when more than one lesion was treated in the same encounter. One patient who presented with SAH and experienced rebleeding during her first trimester of pregnancy was excluded from the analyses of cost of care and LOS, due to extenuating associated medical circumstances that lay beyond her neurological illness and complicated her hospital care.

Treatment Rendered

A standardized care regimen conducted by a single multidisciplinary team over the study period (September 1993–September 1997) ensured consistency in management decisions. Patients were treated in accordance with current guidelines for the management of aneurysmal SAH.^{21,67} This included preoperative diagnostic imaging (CT scanning, magnetic resonance imaging and angiography, and digital angiography), early therapeutic intervention, and aggressive diagnosis and management of neurological and nonneurological complications in a specialized neurosurgical ICU setting. Routine adjuvant therapy included administration of a calcium-channel blocker (nimodipine) and anticonvulsant prophylaxis, intensive management of vasospasm by using hypervolemia and pharmacologically induced hypertension, and, when applicable, the use of external ventricular drainage and shunts for hydrocephalus. Patients with neurological deficits were evaluated for inpatient or outpatient rehabilitation as needed. Aneurysm treatment options included

Impact of GDCs on outcomes in patients with intracranial aneurysms

microsurgical clipping or medical management alone (in unstable or moribund patients) throughout the study period, and the addition of the endosaccular GDC embolization option in the second group. Throughout the series, selected patients, in whom there was a peculiar aneurysm location or configuration, underwent surgical or endovascular parent vessel occlusion, trapping, and so forth, depending on the features and collateral pathways of the individual case.

Surgery and clipping of the aneurysm neck were performed using standard microneurosurgical procedures. Brain relaxation was routinely achieved by a combination of hyperventilation, osmotic diuresis, and cerebrospinal fluid drainage as needed. Temporary vessel occlusion, when used, was managed using intermittent boluses of sodium thiopental aimed at electroencephalographic burst suppression, normotension or hypertension, and mild hypothermia. Intraoperative angiography and selected skull base exposure approaches were used in complex cases. Postoperative control angiography was performed, except in cases of small saccular aneurysms in which the sac was decompressed (incised or punctured) at surgery and in which the surgeon documented circumferential inspection of the aneurysm neck in relation to the applied clip.

The GDC therapeutic option was considered in patients with a medically unstable condition, advanced age, poor clinical grade after SAH, or significant cerebral vasospasm or brain edema, delaying surgery for ruptured aneurysm; on failure of previous surgical exploration or in patients with recurrent or residual aneurysm after prior clipping or endovascular treatment; in anticipation of high risk of surgery due to aneurysm location or configuration; and in response to patient preference. Cases were excluded from GDC consideration if the aneurysm had a broad neck or incorporated the parent vessel or its branches, although this could not always be ascertained until microcatheter exploration was initiated with the intention to treat the aneurysm by using GDCs (that is, preparations for GDC treatment including general anesthesia already instituted). The GDC treatment was performed in the manner described by Guglielmi, et al.,^{33,35} and others.¹⁰⁵ In most cases of ruptured aneurysms, coil embolization was performed immediately after diagnostic cerebral angiography during the same session. Initially, the first several patients undergoing attempted endovascular treatment received awake sedation, although this was subsequently abandoned and general anesthesia was induced in all other patients. General anesthesia was favored for better control of the patient's hemodynamic parameters and clinical condition and potential technical complications. All patients were given anticoagulation therapy at the time of attempted coil embolization by using a bolus of 3000 U intravenous heparin followed by hourly boluses of 1000 U. Post-embolization anticoagulation therapy was continued, in most instances, for 48 hours, unless absolutely contraindicated by ongoing hemorrhage or bleeding diathesis. All patients were monitored in the neurosurgical ICU immediately after GDC treatment and were cared for by the same clinical team mentioned earlier. Only the conventional endosaccular aneurysm obliteration method performed using the GDC system, as originally described,³³⁻³⁵ was used in this group of patients. This period predated the development and implementation of balloon-assisted

neck reconstruction procedures and the third generation three-dimensional coils that subsequently have been developed for endovascular surgical treatment of aneurysms with wider necks.

Effectiveness of treatment (aneurysm obliteration) was documented for each treatment rendered and was graded as verified complete obliteration (confirmed by good-quality postprocedure angiogram), unverified complete obliteration (confirmed only by intraoperative decompression and documented exploration), more than 90% obliteration (residual neck rest or partial sac filling), and less than 90% obliteration.

Data Collection

Host, lesion, and outcome parameters were gathered for each case according to the disease-specific outcome parameters for intracranial aneurysms developed by the Outcomes Committee of the Section on Cerebrovascular Surgery of the American Association of Neurological Surgeons and the Congress of Neurological Surgeons (Aneurysm Outcome Project, Neurosurgery://On Call, www.neurosurgery.org). These include all prognostic variables that have been shown in peer-reviewed literature to affect (univariate or multivariate correlations) patient outcome significantly.^{2,11,22,28,39,43,48,49,52,56,58,63,64,71,73,74,83,85,86,88,97,102-104,106,107,109} Additionally, the physical status of each patient was determined according to guidelines of the American Society of Anesthesiologists^{14,76} based on the medical history and physical examination obtained at hospital admission by one investigator (M.K.S.) who was blinded to outcome. These prognostic factors are listed in Table 1.

Outcome parameters (Table 1) were collected and assessed for the respective treatment of each aneurysm whenever possible.^{4,8,13,15-17,23,25,28,39,41,46,47,51-53,57,59,70,73,75,80,81,85,87,89,91,93,96,99} These included the extent of aneurysm obliteration (as earlier defined), postprocedure incidences of mortality, brain infarcts documented on CT scans (asymptomatic as well as those accompanied by minor or major symptoms), and the GOS scores assigned at discharge from the hospital and at 6 months posttreatment. For each clinical encounter (as defined earlier) we also assessed hospital and ICU LOS, and inflation-adjusted hospital charges as an index of cost of care and resource utilization. We did not attempt to include the cost of professional fees, for inpatient or outpatient rehabilitation or for subsequent outpatient follow-up physical and angiographic examinations.

Statistical Analysis

Data analyses were conducted using a statistical software program (SAS, version 6.12; SAS, Inc., Cary, NC). Student's t-test was used to compare differences between two means, and the chi-square test was used to compare differences between two proportions. Multivariate analyses were also conducted to identify significant predictors of hospital LOS, ICU LOS, total hospital charges (in 1997 US dollars), mortality rate, treatment efficacy, GOS score at discharge, and GOS score at the 6-month follow-up examination. Multiple regression was used for continuous dependent variables, and logistic regression was used for dichotomous dependent variables. In all analyses, to ad-

TABLE 1
List of prognostic and outcome variables

<i>prognostic variables</i>	
patient	
age	
sex	
Hunt & Hess Grades I–V or aneurysm not ruptured	
initial CT scan findings	
Fisher Grades 1–3	
intracerebral hemorrhage	
intraventricular hemorrhage	
hydrocephalus	
American Society of Anesthesiologists physical status score 1–5	
comorbid medical condition	
smoker	
hypertension	
cardiac problem	
aneurysm site (anterior or posterior circulation)	
aneurysm size (<1 cm, 1–2.5 cm, >2.5 cm)	
multiple aneurysms	
<i>outcome variables</i>	
clinical outcome	
GOS score 1–5 at discharge	
GOS score 1–5 at 6 mos posttreatment	
mortality (yes or no)	
brain infarct on CT scan	
no infarct	
yes, but asymptomatic	
yes, minor symptoms	
yes, major symptoms	
LOS	
total hospital LOS from admission	
total ICU LOS	
timing of treatment postevent	
<24 hrs	
24–72 hrs	
3–10 days	
>10 days	
treatment efficacy	
>90% aneurysm obliteration*	
<90% aneurysm obliteration	
hospital charges	
total per admission, corrected for inflation (1997 US\$)	

* Includes all cases of verified complete obliteration (confirmed by good-quality postprocedure angiography), unverified complete obliteration (no adequate postprocedure angiography, but intraoperative visualized obliteration and documented puncture of sac), and cases in which the residual aneurysmal sac filling is less than 10% that of the prior sac volume.

just for inflation, hospital charges for patients discharged before 1997 were converted into 1997 US dollars by using the pricemaster index from the hospital accounting department.

Results

During the study period, 228 intracranial intradural aneurysms were treated at 176 clinical encounters (hospitalizations), with 77 cases managed before the introduction of the GDC procedure (Group I) and 99 managed after its introduction (Group II). There were 32 patients (14 in Group I and 18 in Group II) with multiple aneurysms, including six cases (three in each group) in which different aneurysms were treated in two hospitalizations. Three patients had two separate hospitalizations for the same aneurysm (one in Group I and two in Group II). In this se-

ries, seven patients (four in Group I and three in Group II) were managed conservatively.

In Group II, 27 (27%) of 99 patients underwent treatment or attempted treatment with GDCs. Clinical features of these cases are summarized in Table 2. Twelve of these 27 patients harbored unruptured aneurysms, and one third of the aneurysms treated with GDCs were located in the posterior circulation. In 17 cases GDC treatment was the only modality used to obliterate the aneurysms. In one case an aneurysm neck remnant was retreated with GDCs during a second hospitalization. In six cases the GDC treatment was preceded by surgery performed at another institution (that is, cases of unsuccessful surgery or residual aneurysm). In two additional cases unsuccessful surgical attempts at aneurysm obliteration were made at our institution; one of the patients was subsequently treated with GDC embolization and the other with repeated surgery.

There were six cases in which GDC treatment was attempted but failed (that is, endovascular explorations and/or attempted coil embolizations that ultimately led to aborted treatment because of either technical difficulties or acute complications). Four of these cases were endovascular explorations of intracranial aneurysms that possessed geometric features of uncertain favorability for this therapeutic modality, based on the initial findings in conventional diagnostic catheter angiography. These endovascular explorations were typically pursued as a consequence of either poor conventional therapeutic options or strong patient preferences. Three of the cases in which the intention to treat with GDCs failed were subsequently referred for open surgery. All intention-to-treat failures in the endovascular group were among the first 10 patients referred for GDC treatment. Five patients (18.5%) who underwent treatment or attempted treatment with the GDC system died, three because of initially high Hunt and Hess grade SAHs and the other two because of consequent worsening after periprocedural rupture. Two additional peritreatment hemorrhages occurred without permanent neurological sequelae. The immediate and 6-month functional outcomes of patients treated with GDCs are summarized in Table 2.

Prognostic Variables

Table 3 summarizes the incidence and distribution of the prognostic variables studied for the entire patient cohort and for Groups I and II. There were no significant differences in Group I compared with Group II for these variables except for the incidence of comorbid hypertension, which was greater in Group II ($p < 0.01$). There was a greater prevalence of small aneurysms in Group I ($p < 0.05$).

Outcome Variables

Table 4 shows the incidence and distribution of the outcome variables studied for the entire patient cohort and for Groups I and II. The GOS score at discharge was significantly worse in Group II ($p = 0.046$). Sixty-four percent of the entire cohort had favorable outcomes (GOS Scores 4 or 5) at discharge, and this rate was not significantly different between the groups (69% for Group I and 61% for Group II). At 6 months posttreatment, outcomes were

Impact of GDCs on outcomes in patients with intracranial aneurysms

TABLE 2
Patients who underwent treatment or attempted treatment with GDCs*

Case No.†	Age (yrs), Sex	Aneurysm Site(s)	Size	Other IAs	H&H Grade‡	Indication for GDC Treatment	Discharge GOS Score	6-Mo GOS Score	GDC Efficacy
1	76, F	BA	small	no	—	advanced age, patient preference	3	3	aborted (1)
2	48, F	ICA/paracl	small	no	—	residual aneurysm, patient preference	3	4	aborted (2)
3	63, F	PICA	small	no	V	clinically unstable	3	3	>90%
4	78, F	PICA	small	yes	IV	advanced age, clinically unstable	1	1	>90%
5	30, F	ICA/paracl	small	no	—	high risk technically	5	5	aborted (2)
6	72, F	PCoA	large	no	IV	clinically unstable	1	1	aborted (2)
7	76, F	PCoA	small	no	II	advanced age, clinically unstable	5	5	aborted (2)
8	65, F	BA	small	no	III	clinically unstable, high risk technically	3	3	>90%
9	75, M	BA	small	no	III	advanced age, clinically unstable	3	3	>90%
10	53, M	PCoA	small	no	I	failure of previous surgery, high risk technically	5	5	aborted (2)
11	34, F	ICA/paracl	small	no	—	failure of previous surgery	5	5	>90%
12	68, F	ICA/paracl	large	yes	—	advanced age, high risk technically	5	5	<90%
13	62, F	ICA/paracl	giant	yes	—	high risk technically	5	5	>90%
		BA	small						
		PICA	small						
14	68, F	BA	small	yes	IV	clinically unstable, patient preference	3	4	>90%
		MCA	small						
15	67, F	VA	large	no	—	high risk technically	4	5	>90%
16	78, M	ACoA	small	no	IV	advanced age	1	1	>90%
17	51, F	ICA/paracl	small	yes	—	clinically unstable, failure of previous surgery	3	4	>90%
		ACoA	small						
18	68, F	ICA/paracl	large	yes	—	residual aneurysm	5	5	>90%
19	52, M	PCoA	small	no	IV	clinically unstable	3	3	>90%
20	72, F	MCA	small	no	IV	advanced age, clinically unstable	4	4	>90%
21	68, F	PCA	small	no	—	patient preference	4	5	>90%
22	50, M	ACoA	small	yes	III	clinically unstable	1	1	>90%
23	41, F	PCoA	small	no	—	residual aneurysm	5	5	>90%
24	53, M	ICA/distal	small	yes	—	residual aneurysm	5	5	>90%
25	46, F	ICA/PCoA	large	no	IV	clinically unstable	1	1	>90%
26	78, F	ICA/PCoA	large	no	II	advanced age, high risk technically, patient preference	4	5	>90%
27	44, F	ICA/paracl	small	no	IV	clinically unstable, high risk technically, failure of previous surgery, residual aneurysm	3	4	>90%

* Attempted treatment refers to an intent to treat with GDCs, which was aborted due to complications or technical reasons (treatment efficacy < 90%): (1) = procedure prematurely terminated because of inadvertent P₁ occlusion related to defective device; (2) = endovascular surgery was not possible because of either a wide aneurysm neck or an unfavorable neck/dome ratio. Abbreviations: ACoA = anterior communicating artery; BA = basilar artery; H&H = Hunt and Hess; IA = ischemic attack; ICA = internal carotid artery; MCA = middle cerebral artery; paracl = paraclinoid segment; PCA = posterior cerebral artery; PCoA = posterior communicating artery; PICA = posterior inferior cerebellar artery; VA = vertebral artery; — = unruptured aneurysm.

† In chronological order of GDC treatment.

‡ Pretreatment.

74% favorable overall and there was no difference between the groups (76% of Group I and 73% of Group II). There also was no significant difference between the two groups in mortality rate or infarcts demonstrated on CT scans. The hospital LOS was greater in Group I (20.5 ± 31.9 days compared with 12.5 ± 10.6 days in Group II, $p < 0.05$). The LOS trends (Fig. 1 upper and lower) were evaluated in sequential groups of 20 encounters (20-patient epochs) and sequential 3-month epochs and did not decline after the introduction of the GDC procedure, indicating a general trend of decreasing LOS during the period of the study, starting before and uninfluenced by the introduction of the GDC method. The total ICU LOS also declined between groups (9.2 ± 8.6 days in Group I compared with 6.8 ± 7.1 days in Group II, $p = 0.05$), with a similar trend preceding and uninfluenced by the introduction of the GDC procedure (Fig. 2 upper and lower).

Hospital charges corrected for inflation were lower during the GDC era (Group II) (US \$81,656 \pm 80,649 compared with US \$60,866 \pm 49,106 in Group I, $p = 0.054$),

and again there was no change over time associated with the introduction of the GDC method (Fig. 3). These trends were similar for cases of unruptured and ruptured aneurysms.

During the GDC era, Group II demonstrated an increased frequency for very early treatment (< 24 hours after admission; 12% of cases in Group I and 34% of cases in Group II, $p < 0.05$). Overall, the rate of incomplete aneurysm obliteration (< 90% obliteration) was 12%, and there was no significant difference between groups (8% in Group I and 15% in Group II). In cases treated by surgery alone, the overall unsuccessful obliteration rate was 5.4%, and it did not differ between groups.

Prognostic and Outcome Variables (Results of Multivariate Analysis)

For the whole population, the Hunt and Hess grade was an independent and significant predictor for GOS score at discharge ($p < 0.0001$) and at 6 months posttreatment ($p < 0.0001$), infarct on CT scan ($p < 0.0005$), mortality

TABLE 3

Percentage distribution of prognostic variables among 176 consecutive patients with intradural intracranial aneurysms*

Variable	Percentage of Patients			Difference
	Total (176 patients)	Group I (77 patients)	Group II (99 patients)	
mean age (yrs)†	52 ± 15.3	50 ± 14	53 ± 16	NS
sex				NS
male	30	32	28	
female	70	68	72	
Hunt & Hess grade				NS
no rupture	41	42	40	
I	11	6	15	
II	15	22	9	
III	14	13	15	
IV	12	10	13	
V	7	6	7	
Fisher grade & other findings				NS
1	9	12	7	
2	30	33	28	
3	61	56	66	
intracerebral hemorrhage	11	9	12	
intraventricular hemorrhage	22	28	18	
hydrocephalus	18	17	19	
ASA physical status score				NS
2	15	17	14	
3	24	25	23	
4	57	58	57	
5	4	0	6	
comorbid medical condition				
hypertension	38	26	46	p < 0.01
cardiac problem	16	10	20	p = 0.077
smoker	53	55	52	NS
aneurysm site				NS
anterior	80	80	79	
posterior	20	20	21	
aneurysm size				p < 0.05
<1 cm (small)	46	30	58	
1–2.5 cm (large)	34	43	27	
>2.5 cm (giant)	20	27	15	
multiple aneurysms	18	18	18	NS

* Patients were treated before (Group I) and after (Group II) introduction of GDC embolization. Abbreviation: ASA = American Society of Anesthesiologists.

† Values are the means ± standard deviation.

($p < 0.05$), hospital LOS ($p < 0.0001$), total ICU LOS ($p < 0.0001$), and hospital charges ($p < 0.0001$). Additionally, aneurysm site in the posterior circulation was an independent and significant predictor for GOS score at discharge ($p < 0.05$) and at 6 months posttreatment ($p < 0.01$), treatment efficacy less than 90% obliteration ($p < 0.05$), hospital LOS ($p < 0.005$), and hospital charges ($p < 0.0005$). Larger aneurysm size was an independent and significant predictor of total ICU LOS ($p < 0.01$) and hospital charges ($p < 0.005$). Patient age ($p < 0.05$) and physical status ($p < 0.05$) were independent and significant predictors of patient mortality.

Use of the GDC treatment option was not associated with worse outcome (in any outcome parameter) among Group II cases according to multivariate correlation controlling for age, gender, physical status, clinical grade, and aneurysm site and size.

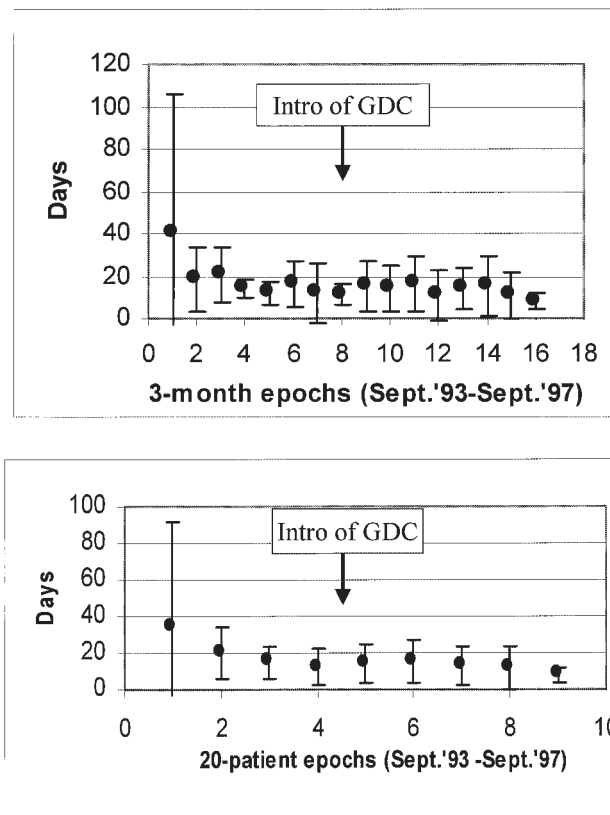


FIG. 1. Graphs displaying trends in hospital LOS per 3-month epoch (upper) and sequential 20-patient epochs (lower) during the study period.

Discussion

Impact of GDCs on Overall Management Outcome

The advantages of the GDC management option over other treatment strategies for intracranial aneurysms have not previously been carefully evaluated. Potential benefits of this modality have been articulated largely on the basis of theoretical and conceptual factors and of treatment outcomes in selected case series without concurrent randomized control groups. More rigorous randomized controlled trials have been hindered by the evolving status of the technology. Also, aneurysm cases advocated for GDC management have largely differed from those selected for surgical treatment. Certain cases unsuitable for surgical treatment because of an unstable medical or neurological condition have been considered for GDC treatment, whereas others have been excluded because of peculiar aneurysm anatomy or geometry (broad-necked aneurysm, an aneurysm sac incorporating the origin of parent vessel branches, and so forth). Hence, it has been difficult to define a subgroup of aneurysm cases for a controlled comparison to assess any potential advantage of the GDC procedure over other treatment options.

With the introduction of a new treatment modality for a subgroup of patients, it may be possible to demonstrate the impact of integration of the new treatment option on overall management outcome. Theoretically, if the pre-

Impact of GDCs on outcomes in patients with intracranial aneurysms

TABLE 4
Percentage distribution of outcome variables among 176 consecutive patients with intradural intracranial aneurysms treated before (Group I) and after (Group II) introduction of GDC embolization

Variable	Percentage of Patients			Difference
	Total (176 patients)	Group I (77 patients)	Group II (99 patients)	
GOS score at discharge				p = 0.046
1	8	4	11	
2	2	4	0	
3	26	23	28	
4	20	26	15	
5	44	43	45	
1-3 (bad)	36	31	40	
4-5 (good)	64	69	61	
GOS score at 6 mos post-treatment				NS
1	9	5	11	
2	1	3	0	
3	16	16	16	
4	15	20	12	
5	59	57	61	
1-3 (bad)	26	24	27	
4-5 (good)	74	76	73	
death	8	4	11	p = 0.08
brain infarct on CT scan				NS
no	57	60	56	
yes, asymptomatic	10	10	9	
yes, minor symptoms	9	10	7	
yes, major symptoms	24	19	28	
timing of treatment				p < 0.05
<24 hrs	25	12	34	
24-72 hrs	30	37	24	
3-10 days	27	26	28	
>10 days	19	26	14	
hospital LOS (days)				
all aneurysms	15.9 ± 22.8	20.5 ± 31.9	12.5 ± 10.6	p < 0.05
ruptured aneurysms	20 ± 27	25.8 ± 38.6	15.6 ± 11.1	NS
unruptured aneurysms	10 ± 12.2	12.7 ± 16	7.9 ± 7.8	NS
total ICU LOS (days)				
all aneurysms	7.9 ± 7.9	9.2 ± 8.6	6.8 ± 7.1	p = 0.05
ruptured aneurysms	10.8 ± 8.6	12.4 ± 9.4	9.5 ± 7.7	NS
unruptured aneurysms	3.6 ± 3.9	4.6 ± 4.1	2.9 ± 3.6	NS
treatment efficacy				NS
>90% obliteration	88	92	85	
<90% obliteration	12	8	15	
hospital charges (1997 US\$)				
all aneurysms	70,023 ± 65,522	81,656 ± 80,649	60,866 ± 49,106	p = 0.054
ruptured aneurysms	88,929 ± 74,364	103,583 ± 94,708	77,739 ± 52,216	NS
unruptured aneurysms	44,194 ± 38,551	52,875 ± 44,124	37,071 ± 32,155	NS
surgery only	72,832 ± 71,327	84,087 ± 84,583	60,827 ± 51,797	NS
GDC treatment only			66,530 ± 46,972	

vailing indications in fact lead to the optimum cases being selected for GDC management (as opposed to surgical or other medical treatment), the introduction of this treatment option would have a positive impact on the overall management outcome of intracranial aneurysms. This hypothesis is impossible to test in a population cohort because the introduction of the GDC modality cannot be standardized or adequately evaluated in a population setting. We examined the hypothesis that integration of the GDC therapeutic option, based on prevailing indications, was associated with improved overall management outcome of intracranial aneurysms at a single institution. We compared management outcome of all cases of intracranial aneurysms at the same institution during the 24

months preceding the introduction of the GDC procedure and during the first 24 months following its introduction. A single multidisciplinary team ensured uniformity of treatment protocols throughout the study period. All clinical data and assessment of disease severity and outcome parameters were conducted by a sole neuroanesthesiologist (M.K.S.), who was not involved in patient selection for surgical or endovascular treatment. This minimizes observer bias, which could have been introduced by surgical or endovascular investigators. Study design and statistical analyses were overseen by collaborators from the Yale-New Haven Hospital Center for Outcomes Research and Evaluation, a group of outcome scientists that does not include neurosurgeons or endovascular therapists.

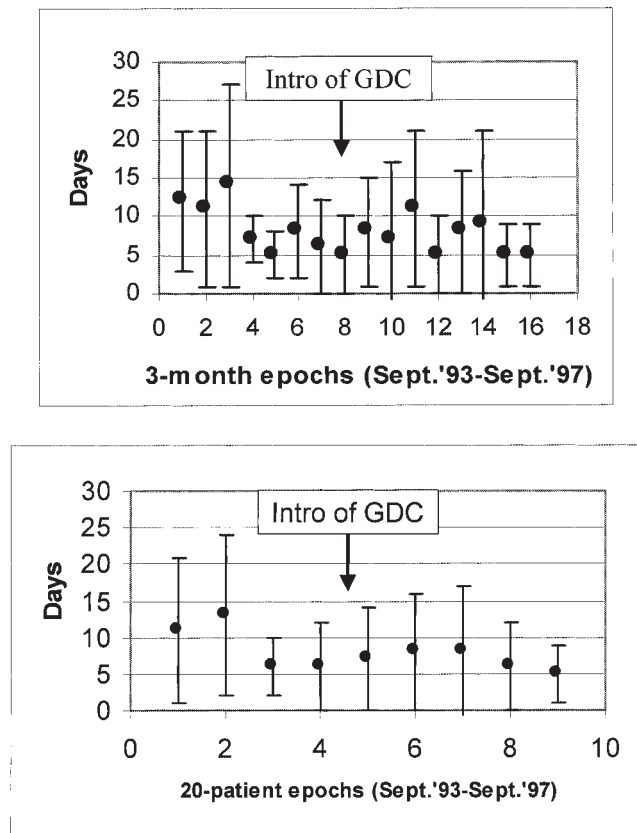


FIG. 2. Graphs displaying trends in total ICU LOS per 3-month epoch (upper) and sequential 20-patient epochs (lower) during the study period.

Our results did not demonstrate any significant impact on clinical outcome, mortality, morbidity, or effectiveness of treatment. Improvements in hospital charges and LOS were shown by epoch trend analysis to be unrelated to the introduction of the GDC therapeutic option.

Potential Biases in the Study Design

There are several potential biases in this study design that may have had an impact on our findings. Our indications for the use of the GDC modality during the first 24 months after its introduction at our institution may not have been optimum. Although the modality was used in 27 (27%) of 99 patients with intracranial aneurysms, the actual patient selection for this endovascular method may have been subjected to considerable referral bias through inconsistent and subjective application of indications criteria, because during this time no formal protocol with precisely articulated definitions of selection criteria was in place. Furthermore, the retrospective analysis of data from this study provides no means of determining whether such a bias occurred. However, the relative utilization of this endovascular option as a percentage of the overall patient population was within the range of reported utilization at many multidisciplinary centers during that time period.^{12,57,65} Furthermore, the indication guidelines for patient

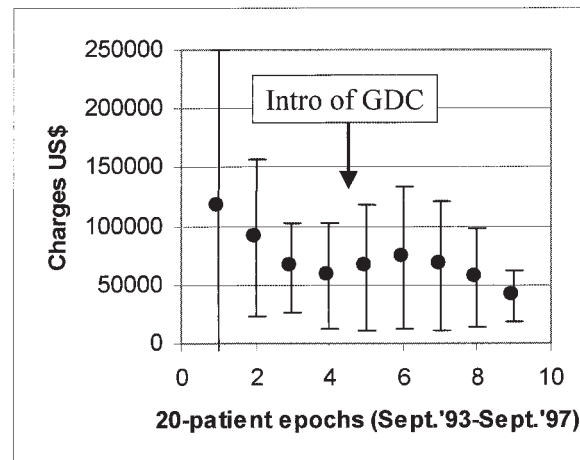
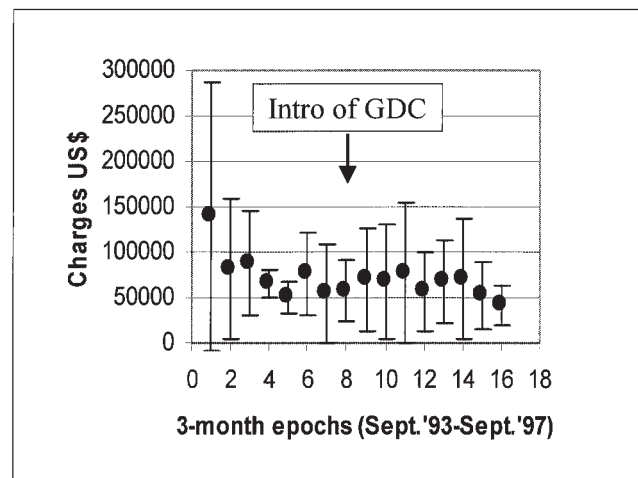


FIG. 3. Graphs displaying trends in total hospital charges (1997 US dollars) per 3-month epoch and sequential 20-patient epochs during the study period.

selection were concordant with those approved by the US Food and Drug Administration and advocated by experts from multidisciplinary centers.

Technical performance with GDCs at our institution and procedure-related incidences of morbidity were well within the range of outcomes reported using this modality,^{12,19,30,50,57,60,65,105} especially when considering the high fraction of elderly patients and patients with unstable medical or neurological conditions selected for this treatment. Endovascular treatment was rendered by an experienced practitioner who had been trained by pioneers of GDC procedure. Special training, proctoring, and other aspects of case management developed this technology. Hence, there is no reason to believe that integration of the GDC procedure at our institution would have incorporated a bias against this treatment that would differ from any other multidisciplinary milieu. Admittedly, the impact of the GDC therapeutic option on overall management strategy might have been more favorable in an environment with less advanced critical care and surgical expertise or in the setting of multidisciplinary teams using indications other than those approved and largely advocated.

Impact of GDCs on outcomes in patients with intracranial aneurysms

The question of a learning curve arises whenever a new technical modality is introduced into the treatment armamentarium. In our experience, two major complications occurred among the very first cases, despite hands-on on-site proctoring by a recognized authority in neuroendovascular therapy. Other procedure-related complications occurred throughout the 2-year period without apparent clustering in the early part of the experience. However, we did observe improved case selection in terms of the feasibility of GDC embolization during later epochs of the study (Table 2). All six cases in which GDC treatment was attempted and abandoned occurred among the first 10 cases in our experience.

The small number of cases in this study may have precluded sufficient statistical power to demonstrate significant differences in outcome between the two groups. Yet the trends (some approaching statistical significance) demonstrated a greater incidence of mortality, worse GOS scores, more infarcts, and decreased treatment effectiveness in Group II (Table 4). Hence, it is unlikely that a benefit of GDC embolization would have emerged with a larger number of cases. A direct comparison of outcomes in GDC-treated cases and surgically treated cases in Group II would not be meaningful because similar cases were not treated by the two modalities.

Disease Severity and Outcome Parameters

This study represents the first comprehensive multidisciplinary experience reported using the outcomes instrument proposed and validated by the Outcomes Committee of the Section on Cerebrovascular Surgery of the American Association of Neurological Surgeons and the Congress of Neurological Surgeons. Disease severity and outcome parameters all appeared to be valid in our cohort when correlated with outcome in univariate and multivariate analyses. The pre-GDC and GDC-era patient cohorts were comparable for major disease severity parameters (patient age, lesion location, clinical grade, and hemorrhage severity), except for slightly smaller aneurysms in the GDC-era cohort (which would have favored better outcome in this group). Treatment was rendered slightly earlier in the GDC-era cohort.

There was apparent benefit in hospital LOS and inflation-adjusted hospital charges (as an index of resource utilization) in the 2-year period following introduction of the GDC technique, compared with the previous 2 years. However, a trend analysis according to sequential 20-patient epochs and 3-month epochs was performed to delineate any trends in hospital stay and charges that occurred during the 4-year period of the study, independent of introduction of the GDC technique. In fact, Figs. 1 through 3 clearly demonstrate that decreasing trends in hospital and ICU LOS and hospital charges occurred well before the introduction of the GDC therapeutic option and were likely unrelated to it.

Comparative Safety and Effectiveness

Despite our findings, we still cannot reliably answer the question of whether the GDC treatment option is safer or more effective than other alternative management strategies for intracranial aneurysms. The advantage or disad-

vantage of GDC therapy compared with surgical treatment in individual aneurysms was not assessed in this study, nor were issues of relative long-term treatment efficacy, specific perioperative medical morbidity, or subtle neuropsychological morbidity. Our study showed no statistical evidence of improved overall outcome in the patient population studied. Additional prospective and randomized studies should be performed to address the efficacy and utility of this endovascular alternative to surgical clipping. We and others are vigorously pursuing the possibility of designing and implementing such a trial in the near future.

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Impact of GDCs on outcomes in patients with intracranial aneurysms

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