Neurochirurgische Auswertung der postoperativen Komplikationen chirurgischer Eingriffe bei pinealen Germinomen (Resektion versus Biopsie) der SIOP CNS GCT 96 Studie

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Abkürzungsverzeichnis

AFP   alpha-fetoprotein

CT   Computertomographie

CNS   Central Nervous System

EVD   external ventrikel Drainage

GCT   Germ Cell Tumors

hCG   human Chorionic Gonadotropin

MRT   Magnetresonanztomographie

ZNS   Zentralnervensystem

1. Deutsche Zusammenfassung

1. Einleitung

Die Inzidenz der intrakraniellen Keimzelltumore im Kindesalter beträgt 0.5 bis 3 % in den USA und in Europa und bis zu 11 % in Asien, insbesondere in Japan, und in Afrika (Echevarría, Fangusaro, & Goldman, 2008).

Am häufigsten treten die intrakraniellen Keimzelltumore zwischen dem 10. und 14. Lebensalter auf, wobei das männliche Geschlecht 2 bis 3-fach häufiger betroffen ist als das weibliche (Hoffman et al., 1991; Jennings, Gelman, & Hochberg, 1985).

Die häufigsten Lokalisationen der intrakraniellen Keimzelltumore sind in der Pinealisloge und suprasellär (Kim, Yoon, Ryu, Jeon, & Hwang, 1998; Tamaki et al., 1990).

Keimzelltumore werden in zwei Subgruppen aufgeteilt, Germinome und nicht-germinomatöse Keimzelltumoren, wobei Germinome den häufigsten Subtyp darstellen.

Die Keimzelltumore stellen mit einem Inzidenzwert zwischen 50 und 75 % die häufigste Tumorentität einer pinealen Raumforderung dar (Echevarría et al., 2008; Kersh et al., 1988; Packer, MacDonald, & Vezina, 2008).

Andere Tumorentitäten in der pinealen Region sind Tumore verschiedener Dignität des Pinealisparanchyms, gefolgt von Gliomen, Ependymomen, embryonalen Tumoren und papillären Tumoren (Hirato & Nakazato, 2001; Kumar, Tatke, Sharma, & Singh, 2006).

Germinome zeigen sich als hochsensibele Tumore gegenüber Radio- und Chemotherapie (Buckner et al., 1999; Douglas, Rockhill, Olson, Ellenbogen, & Geyer, 2006; Haas-Kogan et al., 2003; Jensen et al., 2010; Khatua et al., 2010; Kretschmar et al., 2007). Allerdings sind Germinome in der Regel Marker-negativ, sodass die Diagnose ausschließlich chirurgisch durch histopathologische Untersuchung zu sichern ist. Die

Markernegativität ist in Europa definiert mit Werten für Alpha-Fetoprotein (AFP) unter 25 ng/ml und für Human Chorionic Gonadotropin (hCG) unter 50 IU/l im Liquor und Serum. Die Tumormarker helfen dabei, die reinen Germinome von anderen Tumorentitäten oder gemischten Entitäten zu differenzieren und haben dabei einen Einfluss auf das weitere therapeutische Vorgehen.

Bisher gibt es keine ausführliche Untersuchungen zum neurochirurgischen Vorgehen bei pinealen Germinomen, die die unterschiedlichen Vorgehensweisen der Biopsie bzw. der primären Resektion bezüglich der Vor- und Nachteile bewerten. Einige Studien deuten darauf hin, dass die stereotaktische Biopsie für die Diagnosestellung zuverlässig mit einer Diagnosesicherung zwischen 94 und 100 % ist und nicht mit hohen Komplikationsraten korreliert (Dempsey & Lunsford, 1992; Kreth et al., 1996; Popovic & Kelly, 1993; Regis et al., 1996).
Allerdings können wegen der möglichen Heterogenität der pinealen Keimzelltumoren aufgrund der eingeschränkten Gewebeentnahme Diagnosefehler auftreten (Clark, 1988). Die berichteten postoperativen Komplikationen waren auf eine vorübergehende Verschlechterung der vorbestehenden Symptomatik beschränkt, jedoch wurden auch fatale Komplikationen berichtet (Regis et al., 1996).

Die primäre Resektion bei pinealen Raumforderungen mit dem Ziel einer kompletten Resektion wurde früher in bestimmten Zentren bevorzugt durchgeführt. Als Vorteil wurde angesehen, dass sie sowohl einen diagnostischen als auch kurativen Ansatz bot, da circa ein Drittel der pinealen Raumforderungen benigne ist (Bruce & Stein, 1995; Edwards, Hudgins, Wilson, Levin, & Wara, 1988; Matsutani et al., 1997; Sawamura, de Tribolet, Ishii, & Abe, 1997). Außerdem hat die primäre Resektion den Vorteil, mögliche Probefehlabnahmen zu minimieren und die Tumorgröße deutlich zu reduzieren, sodass eine Liquorableitung durch z. B. eine externe Ventrikel Drainage bei Patienten mit hydrocephalem Aufstau vermieden werden kann (Balmaceda, Modak, & Finlay, 1998; Sawamura et al., 1997). Allerdings weist die primäre Resektion eine hohe Morbiditätsrate von 3-10 % (Bruce & Stein, 1995; Edwards et al., 1988) und Mortalitätsrate von 4-10 % auf (Herrmann, Westphal, Winkler, Laas, & Schulte, 1994).

Im Vergleich dazu beträgt die Morbiditäts- und Mortalitätsrate nach stereotaktischer Biopsie 1-1.3 % (Regis et al., 1996).

Die endoskopische Biopsie ermöglicht eine visuelle Darstellung der anatomischen Verhältnisse der pinealen Raumforderung und des Ventrikelsystems und hilft daher beim Staging. Zudem ermöglicht die endoskopische Biopsie die Durchführung einer Ventrikulozisternostomie zur Behandlung des Hydrocephalus (Reddy et al., 2004).

Aufgrund der oben genannten Vorteile wurde die endoskopische Biopsie in den letzten Jahren bevorzugt (Morgenstern & Souweidane, 2013; Pettorini et al., 2013; Schulz et al., 2020).

Es existiert bisher keine klare und studienbasierte Vorgehensstrategie bei Verdacht auf pineale Germinome (Shabo et al., 2022).

Das Ziel dieser Studie ist die Auswertung und der Vergleich der operativen Eingriffe (Biopsie versus primäre Resektion) bei pinealen Germinomen bezüglich postoperativer Komplikationen und Outcome.

Diese Studie basiert auf der größten prospektiven europäischen Datenbank über intrakranielle Germinome (SIOP CNS GCT 96) und stellt die erste Studie in der Literatur dar, die zwischen Biopsie und primärer Resektion bei pinealen Germinomen vergleicht (Shabo et al., 2022).

2. Material und Methoden

Die Patientendaten wurden aus der internationalen nicht randomisierten Studie SIOP CNS GCT 96 aus 14 europäischen Ländern gesammelt. In der SIOP CNS GCT 96 Studie wurden insgesamt 235 Patienten mit histologisch gesicherten Germinomen von Januar 1996 bis Dezember 2005 eingeschlossen (Calaminus et al., 2013; Shabo et al., 2022).

Von den 235 Patienten hatten 179 Patienten ein unifokales Germinom, von denen 113 pineal und 66 suprasellär lokalisiert waren. Zudem hatten 47 Patienten ein bifokales Germinom und die restlichen 9 Patienten ein metastasiertes Germinom (Abb.1, modifiziert nach Fig.1 nach Shabo, E. et al. in der originalen Publikation).

Die Kohorte der pinealen Germinome (n=113) wurde in 2 Gruppen aufgeteilt: Gruppe 1 (Resektionsgruppe n=58) und Gruppe 2 (Biopsiegruppe n=55). Aus beiden Gruppen waren nach Überprüfung schließlich 57 Patienten in der Resektionsgruppe und 54 Patienten in der Biopsiegruppe auswertbar. Die restlichen 2 Patienten waren wegen inkompletter chirurgischer oder perioperativer Dokumentation nicht auswertbar. Der Altersmittelwert der Patienten betrug 14 Jahre (Minimum 7 und Maximum 42 Jahre).

In der Gruppe 1 wurde die Resektionsmasse anhand postoperativer Bildgebung (CT oder MRT) in 3 Kategorien klassifiziert: totale Resektion, subtotale Resektion >50 % und subtotale Resektion <50 %.
Die Gruppe 2 wurde anhand der Biopsieart ebenfalls in 3 Subgruppen aufgeteilt: stereotaktische, endoskopische und offene Biopsie.

Analysiert wurden bei allen Patienten Erstsymptome, Tumorgröße, durchgeführte chirurgische Eingriffe, postoperative Komplikationen sowie schließlich der prä- und postoperative klinische Status anhand des Lansky- bzw. Karnofsky-Index.

Die Beschreibung der Eigenschaften der Patienten erfolgte entweder als Mittelwert mit Standardabweichung oder Anzahl mit Perzentile. Die Zusammenhänge zwischen Tumorgröße (wie in SIOP CNS GCT 96 klassifiziert: <2 cm, 2-3 cm und >3 cm) und durchgeführten chirurgischen Eingriffen, zwischen Tumorgröße und Erstsymptomatik, zwischen durchgeführten chirurgischen Eingriffen und postoperativen Komplikationen wurden mittels Chi-Quadrat Test und Fisher exact Test analysiert. Die statistische Analyse wurde mittels SPSS Programm, Version 24 durchgeführt. p-Werte <0.05 wurden als statistisch signifikant betrachtet.

3.   Ergebnisse

Die der Untersuchung zugrundeliegende Kohorte besteht aus 111 auswertbaren Patienten mit unifokalem pinealem Germinom (männlich = 106, weiblich = 5). Reine Germinome wurden bei 101 Patienten (91.0 %) diagnostiziert. Die restlichen 10 Patienten (9.0 %) hatten eine Mischung mit Teratom-Komponenten, davon waren 6 Patienten in der Resektionsgruppe und 4 in der Biopsiegruppe.

In der Resektionsgruppe (Gruppe 1, n = 57) erfolgte bei 17 Patienten eine komplette Resektion (29.8 %), bei 14 (24.6 %) Patienten eine subtotale Resektion >50 % und bei 26 (45.6 %) Patienten eine subtotale Resektion <50 % (Abb. 1, modifiziert nach Fig.1 nach Shabo, E. et al. in der originalen Publikation).

Die Erstsymptome in dieser Gruppe waren Hydrocephalus (n = 50 [87.71 %]), gefolgt von Kopfschmerzen (n = 47 [82.45 %]), Parinaud Syndrom (n = 34 [59.64 %]), Doppelbilder (n = 32 [56.14 %]) und Papillenödem (n = 20 [35,08 %]).

Der häufigste operative Zugang war der supracerebelläre infratentorielle Zugang (n = 36 [63.2 %]).

In der Biopsiegruppe (Gruppe 2, n = 54) erfolgte die Biopsie entweder stereotaktisch (n = 39 [72.2 %]), endoskopisch (n = 11 [20.4 %]) oder offen (n = 2 [3.7 %]). Bei den restlichen zwei Patienten existierte keine weitere Dokumentation bezüglich der Biopsieart (Abb. 1, modifiziert nach Fig.1 nach Shabo, E. et al. in der originalen Publikation).

Die häufigsten Erstbeschwerden waren in dieser Gruppe Kopfschmerzen (n = 51 [94.4 %]), Hydrocephalus (n = 43 [79.6 %]), Doppelbilder (n = 30 [55.6 %]), Papillenödem (n = 24 [44.4 %]) und Parinaud Syndrom (n = 23 [42.6 %]).
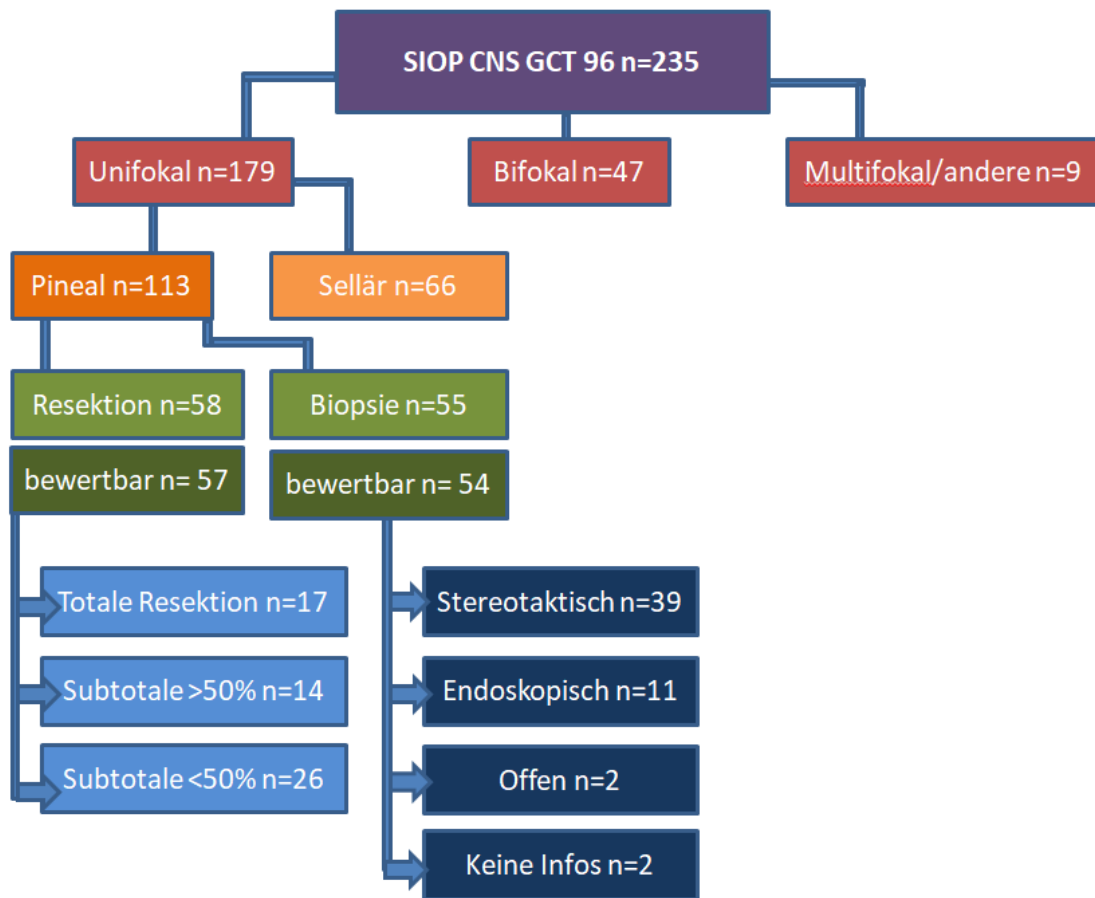
Abb. 1: Patientenkohorte in der SIOP CNS GCT 96 Studie mit weiterer Aufteilung der pinealen Germinome in Resektions- und Biopsiegruppe. (modifiziert nach Fig.1 nach Shabo, E. et al. in der originalen Publikation).

Die Kohorte der pinealen Germinome (n = 111) zeigte als Erstsymptomatik die folgenden Symptome: Kopfschmerzen (n = 98 [88.3 %]), Hydrocephalus (n = 93 [83.8 %]), Doppelbilder (n = 62 [55.9 %]), Parinaud Syndrom (n = 57 [51.4 %]) und Papillenödem (n = 44 [39.6 %]). Es gab keinen signifikanten Zusammenhang zwischen den durchgeführten chirurgischen Eingriffen und den Erstbeschwerden (p>0.05).

Die Tumorgröße wurde insgesamt bei 81/111 (73 %) Patienten dokumentiert, 43 in der Resektionsgruppe und 38 in der Biopsiegruppe.

Die meisten Patienten in der Resektionsgruppe zeigten eine Tumorgröße von 2-3 cm (n = 26 [60.5 %]), gefolgt von einer Tumorgröße >3 cm (n = 10 [23.2 %]) und <2 cm (n = 7 [16.3 %]). In der Biopsiegruppe hatten die meisten Patienten eine Tumorgröße >3 cm (n

= 22 [57.9 %]), 2-3 cm (n = 9 [23.7 %]) gefolgt von <2 cm (n = 7 [18.4 %]) (Tab.1, modifiziert nach Tab.1 nach Shabo, E. et al. in der originalen Publikation).

Es zeigte sich ein signifikanter Zusammenhang zwischen Tumorgröße und dem durchgeführten chirurgischen Eingriff, wobei die Biopsie signifikant häufiger bei großen Tumoren durchgeführt wurde als die Resektion (p = 0.002).

Tab. 1: Zusammenhang zwischen Tumorgröße und chirurgischem Eingriff. Die Biopsie wurde signifkant häufiger bei großen Tumoren durchgeführt (p=0.002). (modifiziert nach Tab.1 nach Shabo, E. et al. in der originalen Publikation).

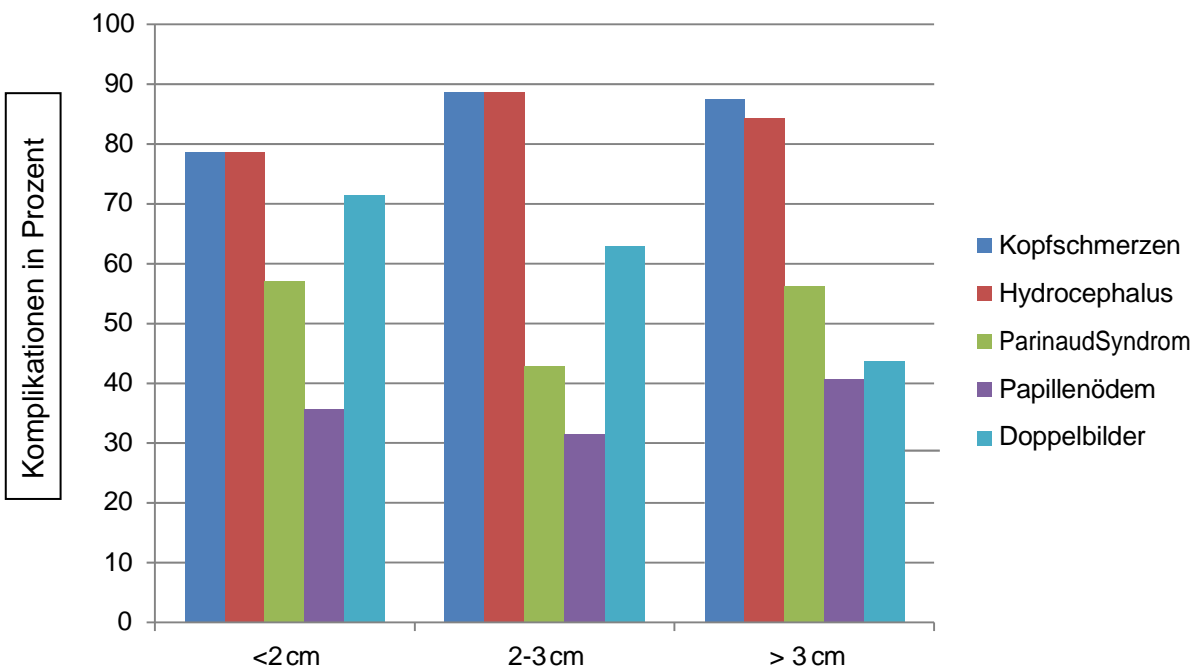|		Resektion	Biopsie	Gesamt	p-Wert (Chi-Quadrat test)
Tumorgröße	<2 cm	7	7	14	
	2-3 cm	26	9	35	
	>3 cm	10	22	32	
Gesamt		43	38	81	0.002

Der Zusammenhang zwischen Tumorgröße und Erstsymptomatik wurde ferner statistisch überprüft (Abb. 2) und (Tab. 2, modifiziert nach Tab. 2 nach Shabo, E. et al. in der originalen Publikation). Hier zeigte sich keine signifikante Beziehung zwischen Tumorgröße und Erstsymptomatik (p>0.05).

Tab. 2: Zusammenhang zwischen Tumorgröße und primärer Symptomatik. Hier zeigt sich keine signifikante Korrelation mit einem p-Wert >0.05 in allen Gruppen. (modifiziert nach Tab.1 nach Shabo, E. et al. in der originalen Publikation)
R=Resektion, B=Biopsie, G= Gesamt

	Tumorgröße<2 cm R-Group n=7 B-Group n=7 Gesamt n=14	Tumorgröße 2-3 cm R-Group n=26 B-Group n=9 Gesamt n=35	Tumorgröße > 3 cm R-Group n=10 B-Group n=22 Gesamt n=32	p-Wert (Chi Quadrat Test)
Kopfschmerzen	R-n=5	R-n=22	R-n=8	
	B-n=6	B-n=9	B-n=20	
	G-n=11 (78,57 %)	G-n=31 (88,57 %)	G-n=28 (87,5 %)	0.090
Hydrocephalus	R-n=6	R-n=23	R-n=9	
	B-n=5	B-n=8	B-n=18	
	G-n=11 (78,57 %)	G-n=31 (88,57 %)	G-n=27 (84,37 %)	0.068
Parinaud syndrom	R-n=6	R-n=11	R-n=7	
	B-n=2	B-n=4	B-n=11	
	G-n=8 (57,14 %)	G-n=15 (42,85 %)	G-n=18 (56,25 %)	0.064
Papillenödem	R-n=0	R-n=9	R-n=5	
	B-n=5	B-n=3	B-n=8	
	G-n=5 (35,71 %)	G-n=11 (31,42 %)	G-n=13 (40,62 %)	0.057
Doppelbilder	R-n=6	R-n=17	R-n=3	
	B-n=4	B-n=5	B-n=11	
	G-n=10 (71,42 %)	G-n=22 (62,85 %)	G-n=14 (43,75 %)	0.050

Abb. 2: Zusammenhang zwischen Tumorgröße und initialen Beschwerden. Es zeigt sich eine ähnliche Verteilung der Erstsymptomatik über alle Tumorgrößen.

Die Häufigkeit der chirurgischen Eingriffe wurde über die Studienjahre analysiert. Die Studie zeigt, dass die Biopsie der pinealen Germinome 1996 und 1997 leicht häufiger durchgeführt wurde als die Resektion (9 Biopsien versus 6 Resektionen). Im weiteren Verlauf zeigte sich eine steigende Tendenz der primären Resektion gegenüber der Biopsie. Zwischen 2001 und 2003 wurden die Biopsie und Resektion fast gleich häufig durchgeführt. Nach 2003 war die Biopsie leicht häufiger als die Resektion. (Abb. 3).
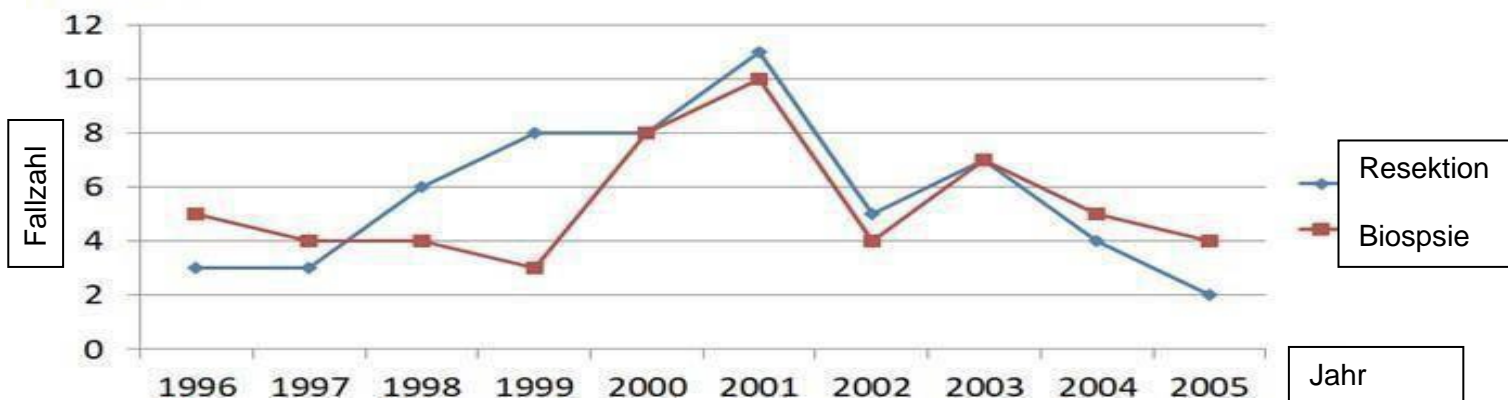

Abb. 3: Die Häufigkeit der Biopsie und der primären Resektion bei pinealen Germinomen basierend auf den Daten der SIOP CNS GCT 96 Studie.

16 Patienten (43.2 %) in der Resektionsgruppe und 5 Patienten (11.4 %) nach Biopsie entwickelten postoperative neurologische Komplikationen (Abb. 4) und (Tab. 3 modifiziert nach Tab. 3 nach Shabo, E. et al. in der originalen Publikation). Die postoperativen Komplikationen traten signifikant häufiger in der Resektionsgruppe auf (p = 0.008).

Tab. 3: Vergleich der postoperativen Komplikationen nach Biopsie und Resektion. Es zeigt sich eine signifikante höhere Komplikationsrate in der Resektionsgruppe (p=0.008). (modifiziert nach Tab. 3 nach Shabo, E. et al. in der originalen Publikation) (modifiziert nach Tab.1 nach Shabo, E. et al. in der originalen Publikation).

			Resektion	Biopsie	Gesamt	p-Wert (Fisher exact test)
Postoperative Komplikationen	keine Komplikationen		21	39	60	
	Postoperative Komplikationen		16	5	21	p=0.008
		Parinaud syndrom/Doppelbilder	9	3	12	
		Hydrocephalus	4	1	5	
		Andere	3	1	4	
Gesamt			37	44	81	
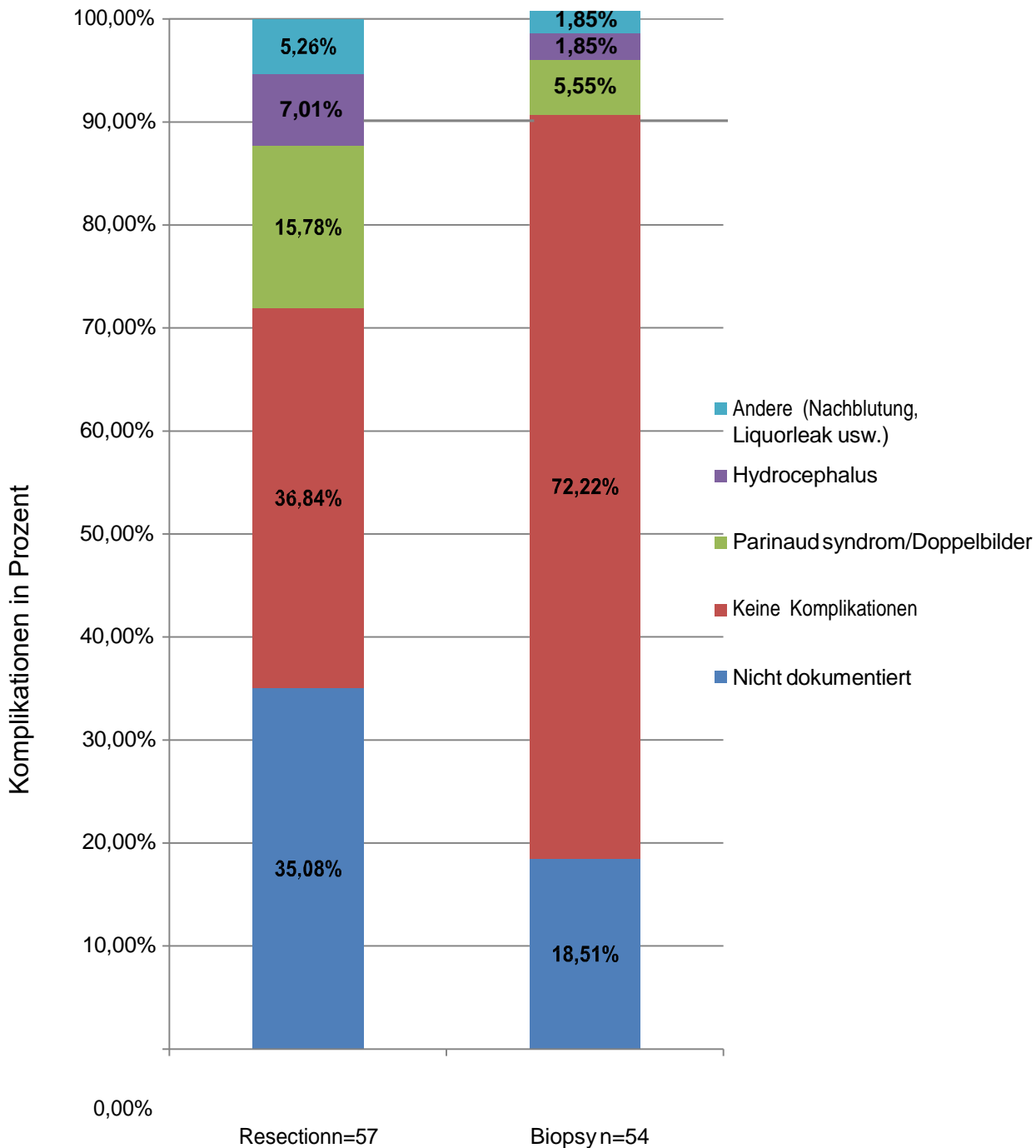
Abb. 4: Darstellung der postoperativen Komplikationen nach Biopsie und Resektion. Es zeigt sich eine deutliche höhere Komplikationsrate in der Resektionsgruppe im Vergleich zur Biopsiegruppe.

Da die häufigsten durchgeführten Zugänge in der Resektionsgruppe der supracerebelläre infratentorielle Zugang und die stereotaktische Biopsie in der Biopsiegruppe waren, war keine sinnvolle statistische Analyse bezüglich

Zusammenhang zwischen ausgewähltem operativem Zugang und postoperativen Komplikationen durchführbar.

4. Diskussion

In dieser Studie werden die perioperativen Verläufe und postoperativen Komplikationen nach chirurgischen Eingriffen (Biopsie versus Resektion) bei unifokalen pinealen Germinomen in der internationalen SIOP CNS GCT 96 Studie zwischen 1996 und 2005 ausgewertet. Die Germinome sind Marker-negativ und die Diagnosestellung kann ausschließlich histopathologisch entweder durch eine Biopsie oder Resektion gestellt werden. Bisher gibt es keine klaren studienbasierten Leitlinien hinsichtlich der Vorgehensstrategie (Biopsie versus Resektion) bei Verdacht auf pineale Germinome (Shabo et al., 2022). Diese Studie soll die Vor- und Nachteile der beiden Prozeduren vergleichen.

Die neurochirurgischen Prozeduren im Bereich der pinealen Raumforderungen waren in der Vergangenheit auf die Behandlung des mitaufgetretenen hydrocephalen Aufstaus beschränkt. Begründet war dies durch die herausfordernde anatomische Lage der Pinealisloge sowie der hohen Sensitivität der pinealen Germinome gegenüber Radio- und Chemotherapie (Marsh & Laws, 1985). Die primäre Resektion wurde initial in wenigen speziellen Zentren weltweit durchgeführt, war jedoch mit erheblichen Morbiditätsraten verbunden (Bruce & Stein, 1995; Herrmann, Winkler, & Westphal, 1992; Konovalov & Pitskhelauri, 2003; Lapras, Patet, Mottolese, & Lapras, 1987; Matsutani et al., 1997; Pendl & Vorkapic, 1985; Stein & Bruce, 1992).

In den letzten Jahrzehnten haben mehrere Studien und Fallberichte gezeigt, dass eine stereotaktische Biopsie zur Diagnosestellung bei pinealen Raumforderungen zuverlässig ist (Balossier, Blond, & Reyns, 2016; Balossier et al., 2015; Pecker, Scarabin, Brucher, & Vallee, 1978).

Der Hydrocephalus ist eine häufige Erstsymptomatik bei pinealen Germinomen. Aufgrund der Entwicklung der endoskopischen Prozeduren insbesondere der Ventrikulozisternostomie wurde die endoskopische Biopsie bei Verdacht auf pineale Germinome wegen ihrer diagnostischen und therapeutischen Vorteile häufiger durchgeführt (Ahmed, Zaben, Mathad, & Sparrow, 2015; Constantini et al., 2013; Fukushima, 1978; Fukushima, Ishijima, Hirakawa, Nakamura, & Sano, 1973; Hayashi et al., 2011; Morgenstern & Souweidane, 2013; Oi et al., 2000; Pople, Athanasiou, Sandeman, & Coakham, 2001; Schulz et al., 2020). Durch ein endoskopisches Vorgehen kann Liquor zur Markertestung sowie eine Probeentnahme von der Raumforderung zur histologischen Aufarbeitung gewonnen werden. Zudem kann der Hydrocephalus durch eine zusätzliche Ventrikulozisternostomie notfallmäßig im gleichen Eingriff behandelt werden. Die berichtete Komplikationsrate nach endoskopischen Eingriffen in der Pinealisloge liegt zwischen 0 und 21.7 % (Ahmed et al., 2015; Schulz et al., 2020).

Die diagnostische Genauigkeit von stereotaktischen und endoskopischen Biopsien wird in der Literatur als akzeptabel beschrieben (Balossier et al., 2016; Balossier et al., 2015; Constantini et al., 2013; Hayashi et al., 2011; Kreth et al., 1996; Schulz et al., 2020), wobei die stereotaktische Biopsie etwas genauer ist als die endoskopische Biopsie (81.1 % versus 93.7 %), jedoch ohne statistische Signifikanz ($p > 0.05$) (Balossier et al., 2015). Die endoskopische Biopsie scheint daher die bessere Behandlungsmethode des Hydrocephalus zu sein und die stereotaktische Biopsie zeigt sich als die bessere diagnostische Methode (Balossier et al., 2015).

Wegen im Vergleich zu Germinomen deutlich geringerer Sensibilität für Strahlen- und Chemotherapie ist die primäre Resektion die bevorzugte Behandlungsmethode anderer Tumoren der Pinealisregion wie z. B. Gliome, Pinealisparenchym-Tumore, embryonale Tumore und Ependymome. Dies wurde in mehreren Studien Anfang 1990 mit einer Mortalitätsrate von 0-2 % und Morbiditätsrate von 0-24 % berichtet (Abecassis, Hanak, Barber, Mortazavi, & Ellenbogen, 2017; Fedorko, Zweckberger, & Unterberg, 2018; Mottolese et al., 2015; Sonabend, Bowden, & Bruce, 2016).

Die Bildgebung und laborchemischen Ergebnisse (Tumormarker) bestimmen bei der Verdachtsdiagnose einer pinealen Raumforderung das chirurgische Vorgehen (Biopsie versus Resektion).

Die europäischen und amerikanischen Protokolle beruhen auf den laborchemischen Ergebnissen (AFP und hCG) als erstem Schritt für Diagnosestellung bei pinealen Tumoren mit dem Ziel, auf eine weitere histologische Sicherung bei positivem Marker zu verzichten. Die histologische Sicherung wird lediglich bei Marker-negativen Tumoren durchgeführt.

Im Gegensatz dazu wird in Japan und anderen Ländern in Asien bei pinealen Tumoren eine primäre Resektion durchgeführt und bevorzugt mit der Begründung, dass die gemischten Keimzelltumoren dort statistisch häufiger als reine Germinome sind und daher die Probefehlentnahme bei Biopsie durch eine Resektion vermieden werden kann (Matsutani et al., 1997).

Im Rahmen einer japanischen Kohorte über intrakranielle Keimzelltumoren wurden Daten von 93 Patienten mit unifokalen Keimzelltumoren der Pinealisregion gesammelt. 26 Patienten davon wiesen einen positiven Marker auf, wobei die nicht-germinomatösen Tumoren histologisch durch einen chirurgischen Eingriff bestätigt wurden, mit Ausnahme eines einzigen Falles mit einem Germinom in der Histologie und AFP von 30 ng/ml im Liquor. In dieser multizentrischen Studie wurden leider keine Angaben bezüglich der postoperativen Komplikationen oder chirurgischen Morbidität berichtet (Takami et al., 2019). Diese Studie hat gezeigt, dass eine im wesentlichen Tumormarker-basierte Behandlungsstrategie den Nachteil hat, Patienten mit einer nicht-sekretierenden nicht-germinomatösen Komponente zu unterbehandeln und Patienten mit reinem Marker-positivem Germinom zu überbehandeln. Diese Tatsache muss bei der Behandlungsplanung ebenso wie die möglichen Risiken der operativen Eingriffe berücksichtigt werden.

Unsere retrospektive Studie zeigt, dass die postoperativen Komplikationen in der Resektionsgruppe im Vergleich zur Biopsiegruppe mit einem p-Wert von 0.008 signifikant häufiger sind.

Bei einer Biopsie können in einem geringen Prozentsatz behandlungsrelevante Tumorkomponenten übersehen werden. Allerdings ist die Biopsie bei Marker-negativen pinealen Tumoren mit klinischem, laborchemischem und radiologischem Verdacht auf ein Germinom der primären Resektion überlegen.

Die Durchführung einer prospektiven Studie zur Evaluation der Vorteile eines chirurgischen Eingriffs insbesondere der primären Resektion bei pinealen Germinomen ist wegen ihrer möglichen erheblichen und unvermeidbaren Risiken sowie der hohen Heilungsrate der pinealen Germinome mittels Radio- und Chemotherapie nicht möglich.

Die Limitationen dieser Studie sind ihr retrospektiver Charakter und die Heterogenität hinsichtlich der Operationstechniken bei Biopsie und Resektion bei fehlendem einheitlichem chirurgischem Standard in den 14 teilnehmenden europäischen Zentren.

5.   Zusammenfassung

Germinome sind der häufigste Subtyp der intrakraniellen Keimzelltumoren und die häufigste Tumorentität einer pinealen Raumforderung im Kindesalter. Germinome sind Marker-negativ und die Diagnosestellung kann ausschließlich histopathologisch erfolgen. Aufgrund der hohen Radio- und Chemosensitivität der intrakraniellen Germinome und aufgrund der statistisch signifikanten niedrigen postoperativen Komplikationsrate nach Biopsie im Vergleich zur primären Resektion sollte bei Verdacht auf pineale Germinome die Biopsie bevorzugt werden.

6.   Literaturverzeichnis der deutschen Zusammenfassung

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2. **Veröffentlichung**

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Article

Evaluation of the Perioperative and Postoperative Course of Surgery for Pineal Germinoma in the SIOP CNS GCT 96 Trial

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Simple Summary: There are many studies that discuss pineal tumors (not specifically germinoma). Some advocate for biopsy over resection due to the fact that germinoma is radio- and chemosensitive; others advocate for primary resection due to multiple differential diagnoses that require resection in the pineal region, such as pineocytoma, teratoma, meningioma, epidermoid, etc. However, with respect to solitary pineal germinoma, there is still no study that analyzes and compares both surgical options regarding peri- and postoperative courses and complications. We evaluated the perioperative course and postoperative complications of patients with isolated pineal germinoma who underwent a primary biopsy or resection, treated according to the European SIOP CNS GCT 96 trial. The key finding of our study was that postoperative complications, including hydrocephalus, Parinaud syndrome, double vision, etc., were significantly higher in patients who underwent primary resection ($p < 0.008$).

Abstract: Background: CNS germinoma, being marker-negative, are mainly diagnosed by histological examination. These tumors predominantly appear in the suprasellar and/or pineal region. In contrast to the suprasellar region, where biopsy is the standard procedure in case of a suspected germ-cell tumor to avoid mutilation to the endocrine structures, pineal tumors are more accessible to primary resection. We evaluated the perioperative course of patients with pineal germinoma who were diagnosed by primary biopsy or resection in the SIOP CNS GCT 96 trial. Methods: Overall, 235 patients had germinoma, with pineal localization in 113. The relationship between initial symptoms, tumor size, and postoperative complications was analyzed. Results: Of 111 evaluable patients, initial symptoms were headache ($n = 98$),

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hydrocephalus (n = 93), double vision (n = 62), Parinaud syndrome (n = 57), and papilledema (n = 44). There was no significant relationship between tumor size and primary symptoms. A total of 57 patients underwent primary resection and 54 underwent biopsy. Postoperative complications were reported in 43.2% of patients after resection and in 11.4% after biopsy (p < 0.008). Biopsy was significantly more commonly performed on larger tumors (p= 0.002). Conclusions: These results support the practice of biopsy over resection for histological confirmation of pineal germinoma.

Keywords: pineal germinoma; resection; biopsy; perioperative course; SIOP CNS GCT 96 trial

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1. Introduction

Intracranial germ cell tumors (GCTs) represent about 0.5 to 3 percent of pediatric central nervous system (CNS) tumors in North America and Europe. By contrast, these tumors are substantially more frequent in Japan and other Asian countries, with a reported incidence of up to 11 percent of pediatric CNS tumors [1]. The peak incidence of intracranial GCT is during the second decade of life, with a median age at diagnosis of 10 to 14 years [2]. There is a male preponderance of between 2:1 to 3:1, especially with tumors in the pineal region [3,4]. Intracranial GCTs arise almost exclusively from midline locations. The two most frequent sites are the pineal and suprasellar regions, with pineal tumors occurring nearly twice as often as suprasellar GCTs [5,6].

GCTs are the most common type of pineal gland tumors [7]. In the literature, the incidence of GCTs varies from 50 to 75% of tumors in the pineal region [1,8,9]. GCTs are further classified into two groups: germinomatous, which is the most common subtype, and nongerminomatous (NGGCTs). Pineal parenchymal tumors are the second most common form of pineal tumors. They represent 14–27% of tumors in the pineal gland [10]. Other CNS tumors can arise from the supporting stroma of the pineal gland and adjacent structures. These tumors include low- and high-grade gliomas, ependymoma, embryonal tumors, pineal parenchymal tumors, and papillary tumors of the pineal region [10,11].

Currently, advanced neuroimaging can provide information to differentiate these entities based on growth pattern and tissue characteristics prior to any intervention, thereby supporting the clinician in deciding on a treatment plan.

Intracranial germinoma are exquisitely radio- and chemosensitive [12–26]. However, in the European protocols (SIOP CNS GCT 96 and SIOP CNS GCTII), surgery to obtain tissue for diagnosis is mandatory for patients with tumor markers below defined thresholds. In Europe, such 'marker-negative' cases are defined by alpha-fetoprotein (AFP) levels below 25 ng/mL and human chorionic gonadotropin (hCG) levels below 50 UI/L, both in the cerebrospinal fluid (CSF) and in the serum. This approach allows pure germinoma or mature teratoma to be distinguished from other benign and malignant lesions.

Of note, the role of neurosurgery (resection versus biopsy) for patients with intracranial GCTs in the pineal region, and its complications, have not yet been thoroughly investigated in large cohorts. Contemporary series suggest that stereotactic biopsy is reasonably safe and well-tolerated [27–30]. Histology obtained by stereotactic biopsy is informative in 94 to 100 percent of cases when multiple target biopsies are obtained, but sampling error may be an issue due to the heterogeneity of pineal GCTs, particularly with mixed histology [31]. Intervention-related morbidity is generally limited to transient worsening of ocular symptoms, although fatal complications have also been reported [28]. A frameless stereotactic robot has also been successfully used for brain biopsies over the past few years [32].

Open surgery rather than stereotactic biopsy, including the option at an attempt for a gross total resection, is favored by some experts as the initial approach to patients with pineal tumors. Because approximately one-third of pineal lesions are benign, open surgery aiming for complete resection of the lesion may be potentially curative as well as diagnostic [33–36]. Furthermore, an open procedure minimizes sampling error, and tumor debulking may obviate the need for CSF diversion if obstructive hydrocephalus

is present [36,37]. However, an attempt for a gross total resection for CNS GCTs is not widely accepted for several reasons. The risk of lasting morbidity from gross total resection is 3 to 10 percent [33,34], while mortality rates range from 4 to 10 percent [38], whereas mortality and morbidity rates for stereotactic biopsy of the pineal region range between 1% and 1.3% [28]. The endoscopic approach with biopsy, also under visual control, in addition to allowing for CSF-sampling, permits direct inspection of parts of the ventricular walls for staging purposes, and allows a third ventriculostomy to be performed for CSF diversion if needed [39].

These aspects and an increased familiarity with neuroendoscopic techniques have led to a shift toward an endoscopic approach for the biopsy of these lesions [40–42]. Any potential benefit from an attempt at an open resection must be balanced against procedural risks.

Although current consensus is to rely on biopsy to diagnose intracranial germinoma due to their high radio- and chemosensitivity, limited systematic and statistical evidence has been provided to support this strategy especially in respect of solitary pineal germinoma [36]. The purpose of this report is to evaluate and compare the perioperative course as well as the postoperative complications of initial primary surgical interventions, namely resection versus biopsy, observed in a large number of patients with solitary pineal germinoma in the international SIOP CNS GCT 96 trial. The evolution of the surgical approach in the presence of a marker-negative pineal mass suggestive of a GCT over the study period was also evaluated.

2. Materials and Methods

Patients' data were obtained from the nonrandomized international SIOP CNS GCT 96 study. A total of 235 patients (176 men, 59 women) with a histologically confirmed diagnosis of a germinoma were enrolled in SIOP CNS GCT 96 from 1 January 1996 through 31 December 2005, and followed up to 18 July 2012 [43].

Of the total 235 patients, 179 had a unifocal germinoma, 113 of which were localized in the pineal region, and the other 66 in the suprasellar region. Forty-seven patients were diagnosed with bifocal and nine patients with metastatic germinomas (Figure 1).
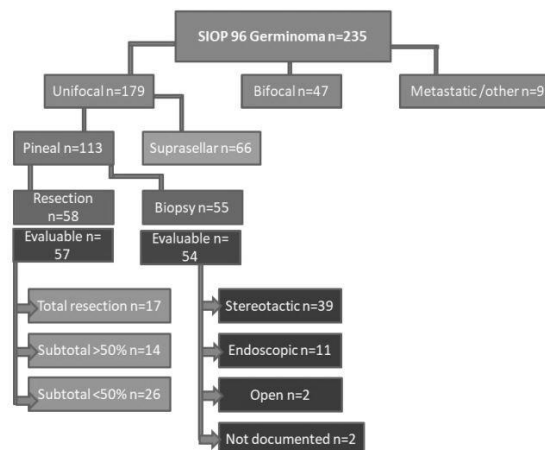
Figure 1. SIOP GCT CNS 96 study patients and classification of two groups (resection and biopsy).

Concerning the contribution of the countries in respect of pineal germinoma, patients were registered from 14 countries. Most patients were registered from Germany n = 32, followed by France n = 20, the United Kingdom n = 17, Austria n = 8, Switzerland n = 7, the Netherlands n = 6, Poland n = 6, Belgium n = 4, Denmark n = 3, Greece n = 3, Italy n = 3, Norway n = 2, Spain n = 1, and Sweden n = 1 (total of 113 pineal germinoma).

In this study, we enrolled all 113 patients with an isolated pineal gland germinoma and divided them into 2 groups: Group 1 (resection group) included 58 patients who underwent a primary resection, and Group 2 (biopsy group) included 55 patients who were initially biopsied.

After reviewing the SIOP CNS GCT 96 database, 57 patients in Group 1 (53 men, 4 women) and 54 patients in Group 2 (53 men, 1 women) were evaluable. The remaining two patients were not evaluable due to incomplete surgical and perioperative documentation. The median age was 14 years (range, 7–42 years).

In Group 1, the extent of resection (EOR) was categorized based on the intraoperative impression of the surgeon combined with results of postoperative imaging by CT or MRI as total resection, subtotal resection (>50%) and partial resection (<50%).

Group 2 was divided into 3 subgroups based on the surgical biopsy technique used (stereotactic, endoscopic, and open biopsy). Initial clinical signs and symptoms, tumor size defined as the largest tumor diameter in any plane, type of surgery, postoperative complications, and pre- and postoperative performance status as assessed by the Lansky/Karnofsky scale were analyzed.

The characteristics of the study patients are described as median values (with range) or numbers with percentages as appropriate. The relation between group and tumor size (categorized in SIOP CNS GCT 96 protocol in the radiological section in <2 cm diameter, 2–3 cm, >3 cm), between groups and primary symptoms and between groups and postoperative complications were assessed by the chi-square test or Fisher's exact test where appropriate. Patients with incomplete documentation were excluded from the statistical analysis. Analysis was conducted using the IBM®SPSS®Statistics (version 25, IBM Corp., Armonk, NY, USA) with p-values < 0.05 considered statistically significant.

3. Results

Of 111 evaluable patients (106 men, 5 women) with unifocal pineal germinoma, pure germinoma was present in 101 patients (91.0%) The other 10 (9.0%) had additional teratoma components: 6 (10.5%) patients were from the resection group and 4 (7.4%) from the biopsy group. No patients presented with other nongerminomatous components.

3.1. Group 1 (Resection Group)

We found that 57 patients had a debulking procedure with a total resection achieved in 17 (29.8%), a subtotal resection (>50%) in 14 (24.6%) and a partial resection (<50%) in 26 (45.6%) patients (Figure 1). The main primary symptoms in Group 1 were hydrocephalus-related (n = 50 (87.71%)), headache (n = 47 (82.45%)), Parinaud syndrome (n = 34 (59.64%)), double vision (n = 32 (56.14%)), and papilledema (n = 20 (35.08%)). The most common operative approach used was the supracerebellar infratentorial approach (n = 36 (63.2%)). Other approaches (e.g., occipital transtentorial (n = 2 [3.5%]), supratentorial transcortical-transventricular (n = 2 [3.5%]), and endoscopic approaches (n = 3 [5.3%])) were less frequently and individually practiced. The surgical approach was not mentioned or documented in 14 patients (24.6%).

3.2. Group 2 (Biopsy Group)

Biopsy-only was reported in 54 patients. Frame-based stereotaxy was used in 39 (72.2%) patients. An endoscopic biopsy was performed in 11 (20.4%) patients, and in 2 (3.7%) patients, biopsy was obtained by an open microsurgical approach. The remaining two patients underwent a biopsy without further information on the technique used (Figure 1).

The main primary symptoms in Group 2 were headache (n = 51 (94.4%)), hydrocephalus-related (n = 43 (79.6%)), double vision (n = 30 (55.6%)), papilledema (n = 24 (44.4%)), and Parinaud syndrome (n = 23 (42.6%)).

Considering both groups combined, the initial symptoms at diagnosis were headache (n = 98 (88.3%)), hydrocephalus-related (n = 93 (83.8%)), double vision (n = 62 (55.9%)), Parinaud syndrome (n = 57 (51.4%)), and papilledema (n = 44 (39.6%)). There was no significant difference between groups concerning primary symptoms (p-value > 0.05).

3.3. Tumor Size

The SIOP committee chose cut-off values for tumor size (<2 cm, 2–3 cm, >3 cm diameter) in the SIOP CNS GCT 96 trial protocol in the radiological finding section and after the section of primary symptoms to evaluate the relationship between primary symptoms

and tumor size.

Tumor size was documented in 81 patients (73.0%): 43 patients in Group 1 and 38 patients in Group 2. The tumor size in Group 1 was <2 cm diameter in 7 patients (16.3%), between 2 and 3 cm in 26 patients (60.5%), and >3 cm in 10 patients (23.2%). Notably, most of the patients in Group 2 had a tumor > 3 cm (n = 22 (57.9%)): nine patients had a tumor size between 2 and 3 cm (23.7%) and the remaining seven patients had a tumor size < 2 cm (18.4%) (Table 1). Tumor size seemed to influence the surgical strategy, with biopsy being significantly more commonly performed on larger tumors (p-value = 0.002).

Table 1. Tumor size and biopsy/resection. Biopsy was the favored operative choice in larger tumors. Using the chi-square test, a p-value of 0.002 was measured.

| | | Biopsy/Resection | | Total | p-Value (Chi-Square Test) |
		Resection	Biopsy		
Tumor size	<2 cm	7	7	14	
	2–3 cm	26	9	35	
	>3 cm	10	22	32	
Total		43	38	81	0.002

3.4. Tumor Size and Primary Symptoms

The relationship between the tumor size and primary symptoms was further analyzed and is summarized in Table 2.

Table 2. Relationship between tumor size and primary symptoms. No significant relationship was found between primary symptoms and tumor size.

| | Tumor Size < 2 cm | | Tumor Size 2–3 cm | | Tumor Size > 3 cm | | p-Value (Chi Square Test) |
	Biopsy	Resection	Biopsy	Resection	Biopsy	Resection	
Headache	6	5	9	22	20	8	0.090
Hydrocephalus	5	6	8	23	18	9	0.068
Parinaud syndrome	2	6	4	11	11	7	0.064
Papilledema	5	0	3	9	8	5	0.057
Double vision	4	6	5	17	11	3	0.050

There was no significant relationship between tumor size and primary symptoms (p-value > 0.05).

3.5. Trends in Surgical Strategy

In 1996 and 1997, biopsy of pineal germinoma was carried out slightly more frequently than resection (nine biopsies vs. six resections), with a decreasing tendency in biopsy until 1999, and an increasing tendency of resection between 1997 and 2001. After 2001, resection and biopsy rates were used with nearly equal frequency, and biopsy has been slightly favored since 2003.

3.6. Postoperative Neurological Status and Complications

Due to incomplete documentation regarding postoperative neurological status and complications, 20/57 (35.1%) patients in the resection group and 10/54 (18.5%) patients in the biopsy group were excluded from the statistical analysis.

Postoperative neurological complications were reported in 16/37 (43.2%) patients after resection, and in 5/44 (11.4%) after biopsy, with total combined complication rate of 21/81 (25.9%) (Table 3). There was a significantly higher proportion of postoperative complications observed in the resection group than in the biopsy group in the documented patients (*p*-value = 0.008).

Table 3. Postoperative complications (biopsy vs. resection). A total of 37/57 patients in resection group and 44/54 patients in biopsy group had complete documentation regarding postoperative complications; the others were excluded from this statistical analysis. There was a significant lower risk of postoperative complications in the biopsy group of the documented patients (*p*-value = 0.008).

		Biopsy/Resection			
		Resection	Biopsy	Total	*p*-Value (Fisher Exact Test)
Postoperative complications	No complications	21	39	60	*p* =0.008
	Postop complications	16	5	21	
	Parinaud syndrome/double vision	9	3	12	
	Hydrocephalus	4	1	5	
	Others	3	1	4	
	Total	37	44	81	

Two of the five patients in the biopsy group who developed postoperative complications underwent a stereotactic biopsy, and the other three patients underwent an endoscopic biopsy. Of the 16 patients in resection group with postoperative complications, 6 underwent partial resection, 4 subtotal, and 6 total resection.

As the vast majority of the patients underwent either a resection by an infratentorial-supracerebellar approach or a stereotactic biopsy, statistical analysis of the complication rates with regard to the approach chosen within the resection and biopsy groups respectively was not feasible due to high differences in case numbers.

4. Discussion

We analyzed the perioperative course in relation to the type of surgery for all patients diagnosed and treated for germinoma of the pineal region within the SIOP CNS GCT 96 study. These initial tumor-targeted surgeries were performed between 1996 and 2005 in 14 European countries, reflecting treatment in numerous neurosurgical units. The neurosurgical protocol guidelines, although highlighting the need to obtain tissue in marker-negative tumors, did not clearly specify the type of surgical approach that should be employed. For this reason, the reported data reflect the current practices for the initial neurosurgical approach in these patients, who commonly present for diagnosis at the neurosurgical unit with acute hydrocephalus.

The rate of postoperative complications/worsening was significantly higher in the group that underwent a debulking procedure than in those who underwent biopsy-only interventions, the majority of which were performed using a stereotactic or an endoscopic technique (*p* = 0.008).

Historically, the neurosurgical approach to these tumors was limited to treating the associated hydrocephalus [44] due to the technical difficulties in the surgical approach to tumors in the pineal region, the majority being germinoma on histological examination, and their excellent response to radiotherapy. Tumor removal was initially confined to selected centers of expertise that could show that resection was feasible with acceptable morbidity [33,35,45–49].

Over the last few decades, reports have shown that using a stereotactic biopsy approach as the initial diagnostic procedure is safe and reliable [50–52], an observation that has been reproduced in multicenter studies [28,52]. However, there are no systemic studies

that statistically compared primary resection and biopsy on solitary pineal germinoma. Even without an underlying statistical analysis, the current existing literature slightly recommends biopsy over primary resection of pineal germinoma based on the high radio- and chemosensitivity of germinomas. Furthermore, many studies recommend primary resection for solitary pineal tumors due to possible differential diagnosis tumors, which require radical resection, such as pineocytoma, teratoma, meningioma, epidermoid, etc. [36].

With obstructive hydrocephalus being present in the majority of patients, and with endoscopic ventriculocisternostomy becoming favored as the treatment of choice, combining this procedure with a transventricular endoscopically guided biopsy became increasingly used [40,42,53–59]. Within the SIOP CNS GCT 96 study, NGGCTs made up 42% of tumors occurring in the pineal location. With endoscopic third ventriculostomy as the favored technique for treating the associated hydrocephalus, this approach offers the opportunity for sampling CSF for markers while obtaining a biopsy specimen within the same intervention, and has a reported rate of complication between 0 and 21.7% [40,59]. If serum markers are not be available at the time of an urgently needed intervention, and with CSF markers not yet having been performed, the surgeon would need to balance the risks of performing an ultimately redundant biopsy and the benefits of potentially avoiding the need for a second procedure.

The diagnostic yield and accuracy are generally deemed acceptable with both stereotactic and endoscopic techniques [27,40,50,52,55,56]. Nevertheless, tissue diagnosis may be less accurate with endoscopic than with stereotactic procedures (81.1% versus 93.7%), though without reaching statistical significance ($p > 0.05$) [52]. Thus, although the neuroendoscopic approach seems to be the best tool for managing hydrocephalus, stereotactic biopsies may represent the best way to obtain a tissue diagnosis with accuracy and low morbidity [52].

Conversely, an attempt at resection is currently deemed appropriate for most non-GCT pineal tumors such as glioma, pineal parenchymal tumor, CNS embryonal tumor, and ependymoma.

In a series of patients treated from the 1990s on, complication rates for pineal tumor surgery were about 0–2% for mortality, 0–5% for major morbidity, and 0–24% for minor morbidity for such entities [60–63].

Most surgical series of resection of pineal tumors of various histologies with sufficient detail on postoperative follow-up report on the experience of single institutions, often even single surgeons [64]. Postoperative morbidity of resective procedures in recent monoinstitutional series ranges between 19% and 22% [33,35,41,49,62,63,65–67], with up to 45.6% adverse events in the period of 30 days after surgery [68]. The finding of a 43% complication rate after resection within the SIOP CNS GCT 96 trial could be related to its multicenter/multisurgeon database. An additional factor to take into account when comparing our results with those of other series is the infiltrative nature of germinomas compared with other histological entities encountered in the pineal region. Most of the series pool these heterogeneous pathologies when reporting on complications.

Advanced neuroimaging combined with clinical information can contribute to the prediction of the tumor type and guide decision making. This may not only impact the eventual surgical approach used, but, more importantly, the management guidelines for the working diagnosis that determine the need for resection as part of treatment versus valid histological sampling only.

Whereas study protocols in Europe and North America increasingly relied on AFP and HCG to diagnose and stratify GCT, obviating the need for histological confirmation in cases with typical radiology and elevated markers, and mandating histology for marker-negative cases only, most Japanese and other East Asian groups continue to favor primary extensive resections in pineal tumors. Due to a much higher incidence of CNS GCTs in these regions, this approach was supported by documenting the histological heterogeneity and high percentage of mixed histology GCTs, thus highlighting the risk of a sampling error with a small biopsy specimen [35].

Within the SIOP CNS GCT 96 study, of the 113 patients with unifocal pineal germinomas, 1/54 initially diagnosed with a biopsy had a local relapse with a diagnosis of the NGGCT subtype yolk sac tumor (YST) [43]. One could argue that a YST component had been missed in the biopsy specimen of the initially marker-negative tumor (i.e., alpha-fetoprotein (AFP) below 25 ng/mL and human chorionic gonadotropin (hCG) below 50 UI/L in both compartments).

Within the cohort of the Japanese intracranial GCT (iGCT) Consortium, data from 93 patients with a unifocal GCT of the pineal region were collected. Twenty-six had markers elevated above the SIOP CNS GCT 96 cut-off values, with the nongerminomatous diagnosis confirmed by surgery, except for a single case with a germinoma at biopsy and AFP of 30 ng/mL in CSF. Two patients had a YST diagnosis without markers available. Of the remaining 65 patients, biopsy-only was performed in 22 cases, and a resection in 43. Two patients undergoing resection were diagnosed as mixed germinoma-embryonal carcinoma. No information on surgical morbidity was provided for this multicenter study [69]. Therefore, a tumor-marker-based strategy has its pitfalls: it is possible to undertreat patients with a nonsecreting NGGCT component, and overtreat patients with a pure germinoma that has tumor markers above the defined thresholds. This potential pitfall must be balanced with the possible morbidity of surgery.

The high cure rates for patients with pineal germinomas using current protocols are a major impediment to assessing a potential therapeutic benefit to upfront resection for such cases, with its associated with unavoidable risks, in any potential prospective study [43]. Despite the low risk of missing a treatment-relevant tumor component in a biopsy procedure, our data support the practice of biopsy-only as the primary surgical approach to marker-negative pineal region tumors with clinical/radiological suspicion of germinoma.

The limitations of this study are its retrospective nature and the heterogeneity of the surgical techniques used for biopsy and resection procedures. This heterogeneity could at least partly be related to the shift in neurosurgical approach from a center-specific standard approach to a more widespread implementation of image-guided biopsy and endoscopic techniques.

5. Conclusions

With the excellent sensitivity of CNS germinoma to chemotherapy and/or radiation, the neurosurgical role for germinoma needs to be very carefully evaluated. With limited evidence for the benefit of an upfront debulking procedure, biopsy-only of localized suspected germinoma in the pineal region should be favored over primary resection due to the significantly lower risk of surgical postoperative complications.

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