MANAGEMENT AND OUTCOMES OF PEDIATRIC NEUROENDOCRINE TUMORS – A SYSTEMATIC REVIEW OF PUBLISHED STUDIES

Oona Tasto, MD [1]

Arimatias Raitio, MD, PhD [1]

Paul D Losty, MD FRCSI FRCS(Ed) FRCS(Eng) FRCS(Paed) FEBPS [2,3]

1. University of Turku and Turku University Hospital, Paediatric Surgery, Turku, Finland
2. Institute Of Systems Molecular And Integrative Biology, University of Liverpool, Liverpool, UK
3. Department of Paediatric Surgery, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Corresponding author:

Professor Paul D Losty MD FRCSI FRCS(Ed) FRCS(Eng) FRCS(Paed) FEBPS

Institute Of Life Course and Medical Sciences,

University of Liverpool, UK

Email Paul.Losty@liv.ac.uk

Declaration of Competing Interest

Dr Raitio reports research grants from Päivikki and Sakari Sohlberg Foundation.

Abstract

Neuroendocrine tumors (NETs) are rare in the pediatric age group with studies reportedly showing increased incidence in females. The appendix appears to be the most common tumor site, but NETs can arise almost anywhere in the body. Due to rarity, comprehensive reports detailing outcomes are sparse and often based on limited index case numbers. This study aims to systematically analyze outcome metrics of pediatric NET whilst identifying pertinent risk factors for mortality. Medline/Embase databases were searched according to PRISMA guidelines. Final analysis included 83 studies with 3,829 NET patients (1,917 females – 52%). Individual patient data was available in 522 patients (49 studies) with a mean follow-up period of 67 months. The most common tumor sites included appendix (30%), adrenal gland (19%), pancreas (19%), and bronchus/lungs (14%). Surgical tumor resection was the mainstay of treatment while 23 patients (5%) were managed medically. Recurrence(s) were observed in 35 patients (8%). Chemo/radiotherapy was reported in 48 patients (12%). Most patients (94%) survived - 86% (n=378) with no evidence of disease, 8% (n=37) were alive with disease and 29 (6%) died of progressive disease. Positive margins at primary operation, metastatic disease, and large tumor size were associated with mortality (p=0.0006, <0.0001, and 0.018, respectively). Significantly higher mortality was observed with NETs originating from the liver and thymus. These findings affirm that despite predominantly favorable outcome, complete surgical resection (R0) is crucial, as positive surgical margins predispose to mortality. Similarly, larger tumor size and certain anatomical tumor sites are associated with worse outcome(s).

Keywords: neuroendocrine tumor; pediatric; NET;

Abbreviations: NET – neuroendocrine tumor

1. Introduction

Neuroendocrine tumors (NETs) are typically considered as benign tumors but have the potential to transform into a malignant form [1]. NETs are rare in the pediatric population, Navelke et al. reported an incidence rate of 2.8 per million in children and young adults less than 30 years of age [2]. However, it has been pointed out that there is an increase in the prevalence and incidence of NETs, probably due to improved diagnosis [3].

Over 90% of the NETs found in children are located in the appendix but tumors can arise from neuroendocrine cells anywhere in the body [4]. It has been reported that 10-20% of these tumors in the pediatric population are metastatic at diagnosis [2].

Symptoms depend on the site and size of the tumor. Appendiceal tumors typically present with acute abdominal pain from appendicitis [1]. They are seldom metastatic and are considered to have an excellent overall survival approaching 100% [5].

The most common pulmonary tumors in the pediatric population are bronchial NETs [4]. At an early stage, patients are often asymptomatic, so diagnosis is often established after clinical symptoms are later evident. Symptoms include coughing, dyspnea, chest pain, wheezing and nearly 50% of these patients will present with pneumonia [6]. Carcinoid syndrome is rare in the pediatric population as most young patients do not have metastatic disease to the liver [6].

Surgery, notably tumor resection, is the first line of management for localized NETs [7,8]. However, complete resection is often not possible in those with metastatic

disease [1]. Whilst all NETs will mandate resection, residual local disease and metastases may remain [6]. For these patients treatment options may include somatostatin analogs, molecularly targeted therapy, cytotoxic chemotherapy, and peptide receptor radionuclide therapy (PRRT) [1].

Neuroendocrine tumors are thus uncommon in the pediatric population, consequently comprehensive reports detailing outcomes are often based on limited index case numbers. The aims of this systematic review were therefore firstly to systematically analyze (i) clinical outcome metrics of pediatric NET and secondly (ii) identify risk factors for mortality.

2. Material and methods

2.1. Identification and selection of studies

According to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, a comprehensive search in PubMed and Embase databases was performed using the following terms as keywords: ‘Neuroendocrine Tumo(u)r’ in combination with terms ‘child’, ‘p(a)ediatric’, ‘outcome(s) ’, ‘adolescent’. All articles published up to January 10 2025, were included in the final study review.

2.2. Inclusion and exclusion criteria

We included all articles with outcomes of pediatric NET (0–18 years) in the study. During the title and abstract screening, we excluded papers with case reports (<3 patients) and papers that were not available in English language. Papers where

pediatric patients could not be analyzed separately from adults and those where NET could not be analyzed separately from other varied diagnoses were not included. Also, manuscripts with insufficient (N) numbers (<3) of pediatric NET patients were similarly excluded. (Figure 1)

2.3. Data extraction and analysis

The included articles were independently reviewed by both study authors (OT & AR) and final selection approved by the senior author (PDL). The extracted data included patient sex, age, tumor location and size, potential metastasis, treatment, potential recurrence (either local or distant), length of follow-up, outcome (s), and mortality. Surgical resection was defined as complete (no residual tumor with clean margins) or incomplete (residual tumor and/or tumor extension to resection margin) where available. Both microscopic and macroscopic margins were included. Survival was defined as the overall survival of the whole follow-up period.

2.4. Statistical analysis

Chi-Square and Fisher's exact tests were utilized to analyze categorical variables. Kaplan-Meier analysis was used for survival analysis and multivariable logistic regression for risk factors for mortality. A significance level of $p \leq 0.05$ (two-tailed) was set. Analyses were performed using JMP Pro, version 18.2.1 for Windows (SAS Institute Inc., Cary, NC, USA).

3. Results

We undertook a systematic review through different databases and identified 6761 studies. After duplicates were excluded, 5821 studies were then evaluated. Inclusion criteria were met in 234 papers after screening the titles and abstracts, of which four were not able to be retrieved. In total 230 papers were thus assessed. Inclusion criteria were met in 83 papers with 3,829 NET patients (1917 females – 52%) (Figure 1). The papers that were included in the final study were published from 1946 to January 10th, 2025. Individual data was available in some 49 studies encompassing 522 patients and the number of individual patients in different studies ranged from 3 to 31 [5,9-56] (Supplementary table). The mean follow-up period was 67 months.

In our systematic review, the overall survival rate was 93.2%. The most common tumor sites included appendix (30%), adrenal gland (19%), pancreas (19%) and bronchus or lungs (14%). Whilst pheochromocytoma are included among the broader and wider classification of NET tumors in the pediatric age group debate with regard classification and outcomes may be varied in adult populations. Tumor site had a major role in influencing survival ($p<0.001$), thymus (37.5%), liver (50%), gastrointestinal tract excluding the appendix (75%), adrenal gland (92.7%), pancreas (93.6%) and appendix (99.4%) – Figure 2. However, the total number of patients overall was small, regarding tumors located in the thymus, liver and gastrointestinal tract excluding the appendix - Table 1.

Surgical tumor resection was the mainstay of treatment in most patients (95%), while the remaining cases were managed medically. Recurrence was observed in 35 patients (8%), with 27 (7%) requiring surgery. Recurrence rates were notably associated with the tumor site ($p=<0.0001$). Highest recurrence rates (%) were

observed with tumors in the thymus (42.9%), liver (40%), gastrointestinal system excluding the appendix (20%), parathyroid (16.7%), adrenal gland (14.6%) and bronchopulmonary sites (10.9%). No statistical differences were associated with recurrence (%) after positive margins at primary operation (p=0.07).

Adjuvant treatment, either chemo or radiotherapy was administered to 48 index patients (12%). Overall, 94% of patients survived, with 86% (n=378) having no evidence of disease, 8% (n=37) were alive with disease at follow up and 29 (6%) died of progressive disease. Overall survival was reassuringly excellent, but certain tumor sites, especially liver and thymus, were associated with significant mortality (Figure 2).

In univariate analysis, large tumor size was associated with a higher mortality (p=0.018), also positive margins at primary operation (p<0.001), and metastatic disease (<0.0001) were notably associated with poorer prognosis. There were no significant differences found in survival (%) depending on patient age (p=0.74) or sex (p=0.33). We also noted no significant difference(s) in recurrence rate (%) according to sex or age (p=0.60 for both). In multivariable analysis, only metastatic disease was a significant predictor of mortality (p=0.04) and large tumor size for recurrence (p=0.01). In subgroup analysis, there were 28 mortalities among 343 patients with extra-appendiceal NET lesions while only one death was reported in 159 appendiceal NETs, p<0.001). Also, mortalities were significantly more common in those with metastatic (46%) vs. localized disease (2.3%), p<0.001 – Figure 3).

Tumor site	Number of patients (%)	Mortality (%)
Appendix	159 (30.5)	1 (0.6)
Extra-appendicular tumors	363 (69.5)	28 (8.2)
Adrenal gland	100 (19.2)	7 (7.3)
Pancreas	99 (19.0)	6 (6.4)
Bronchus / lungs	71 (13.6)	2 (3.1)
Thyroid gland	32 (6.1)	0
Parathyroid gland	12 (2.3)	0
Liver	9 (1.7)	3 (50.0)
Thymus	8 (1.5)	5 (62.5)
Other gastrointestinal site(s)	8 (1.5)	2 (25.0)
Localized tumor	442 (91.9)	10 (2.3)
Metastatic disease	39 (8.1)	16 (41.0)
Total	522	29 (5.8)

Table 1: NET tumor sites and reported mortality (%)

4. Discussion

Pediatric NET are typically very rare tumors that in most cases are benign in nature. In this systematic review study, the overall survival rate was 93.2%. Ankestjerne et al. recorded a zero-mortality rate in their report from Denmark covering the study period 1995-2020 [4]. The appendix is the most common site of origin for pediatric NET tumors which is compatible with prior limited pediatric reports [4,23,57]. This systematic review study shows that anatomical tumor site is the most important prognostic factor for patients. In multivariable analysis, metastatic disease was the

only significant prognostic factor. Recurrence of tumor is also highly dependent on the tumor site origin, both of which were also recorded by Degnan et al. [19].

Certain anatomical sites such as the thymus gland and liver are associated with poorer prognosis. In the adult population the survival rate of thymus NET is highly dependent on histological stage and are more often higher-grade lesions, with the 5-year survival varying from 30–100% depending on the histology [58]. NET of the liver are rare also in the adult population and therefore clinical characteristics and survival outcomes are still not fully understood. Li et al. assessed a SEER database and found that poorly differentiated tumor grades and no surgery were associated with poorer prognosis, as well as patient age and unmarried status [59]. The survival of adult patients with pancreatic neuroendocrine tumors has increased over time, with no clear reasons [60]. A large population-based study using SEER data suggested that the functional status of the tumor is an independent prognostic factor. In a separate study authors report that overall survival in all cases was 28 months [60]. In our current study we observed an overall survival of 94%, which may be influenced in part by sparsity of individual data in several papers on pancreatic NET. Similarly, the observed poorer survival with liver and thymus gland NETs, are likely based on a small number of index patients, which may increase the risk of bias. Appendiceal NET tumors in the pediatric age groups in this current systematic review study and now more recent published work continues to carry an excellent prognosis reaffirming our investigative findings [61,62].

Virgone et al. comprehensively reviewed the Italian TREP database comprising patients harboring extra-appendicular NET tumors for the study time period 2000-2020 [55]. They reported that localized disease and complete surgical resection were major prognostic features. In our current study we did not find any significant difference(s)

with recurrence (%) associated with positive margins found at primary operation. However, our data have shown that positive margins and metastatic disease were associated with higher mortality.

The need for adjuvant treatment in the pediatric population is rare [23]. Virgone et al. claimed that it is difficult to accurately determine the effects of multimodal therapies including chemotherapy or somatostatin analogs on survival [55]. Some 12% of index patients in the current study appeared to receive adjuvant treatment.

The size of NET tumor in this systematic review study was notably associated with tumor recurrence (%). Venara et al. in a publication in 1998 noted that tumor size alone did not seem to be a reliable outcome predictor in adrenal cortical NET tumors [54]. Degnan et al. in 2017 recorded from their retrospective study analysis and review of 45 cases that tumor size independently corresponded with recurrence (%) and metastases [19]. However reassuringly in appendiceal NET tumors, appendectomy is associated with excellent long-term survival, regardless of tumor size. Similar favorable outcomes were reported in 2016 in a study from de Lambert et al. [63].

In this systematic review we found that there were no significant differences in recurrence rates (%) depending on sex or patient age. Ankestjerne reported a female predominance [4] as did Degnan et al. specifically with regard bronchial NET [19]. However, with regard appendiceal NET neoplasms male vs female gender rates were equivalent and with extra-appendiceal tumor sites there was a predominance in the male population [19]. In this current systematic review study some 52% of index cased were female. We found in this report there were no significant differences noted in tumor location dependent on patient sex.

To the best of our knowledge, this is the first comprehensive systematic review study seeking to better understand the unique characteristics and behavior of NET tumors in the pediatric population. We fully acknowledge there are certain inherent limitations to the current study including variations in after care follow up of patients, methods of data reporting, and incomplete data on individual patients.

5. Conclusion

NETs are rare tumors in the pediatric population with predominantly a favorable outcome. Probably due to improved diagnosis, the incidence and prevalence rates appeared to have increased. Complete surgical resection (R0) is crucial, as positive surgical margins may predispose to mortality. Similarly, larger tumor size, metastatic disease burden and certain anatomical tumor sites are associated with worse outcome(s).

Author contributions

The study was originally conceived and designed by PDL. OT and AR conducted the literature review, data collection, analysis, and interpretation under supervision by PDL. The manuscript was drafted by OT and AR. All authors participated fully in drafting the manuscript, revisions and approved the final version submitted manuscript.

Declaration of Competing Interest

Dr Raitio reports research grants from Päivikki and Sakari Sohlberg Foundation. Funder had no role in the current study.

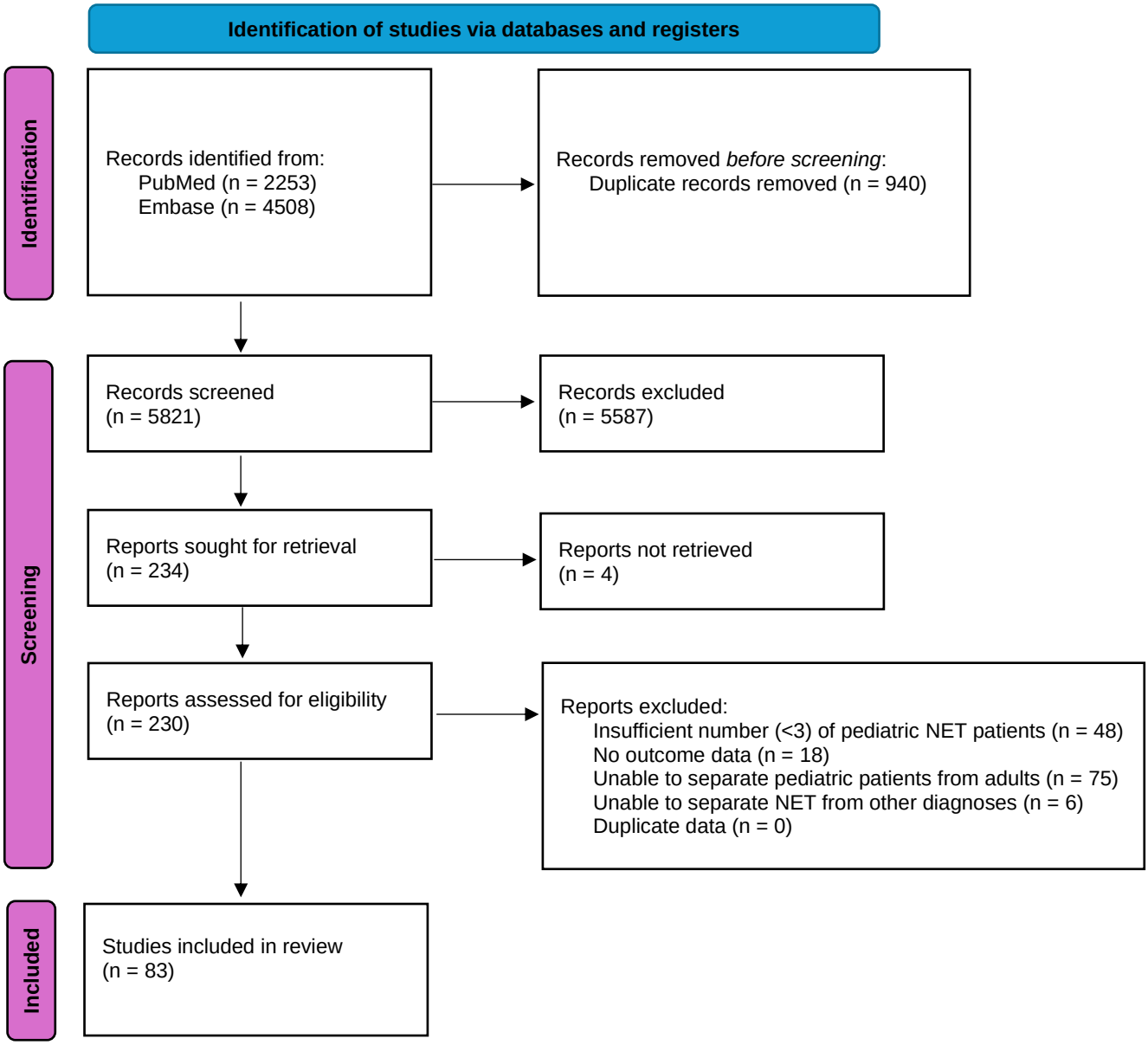

Figure 1. PRISMA flow chart

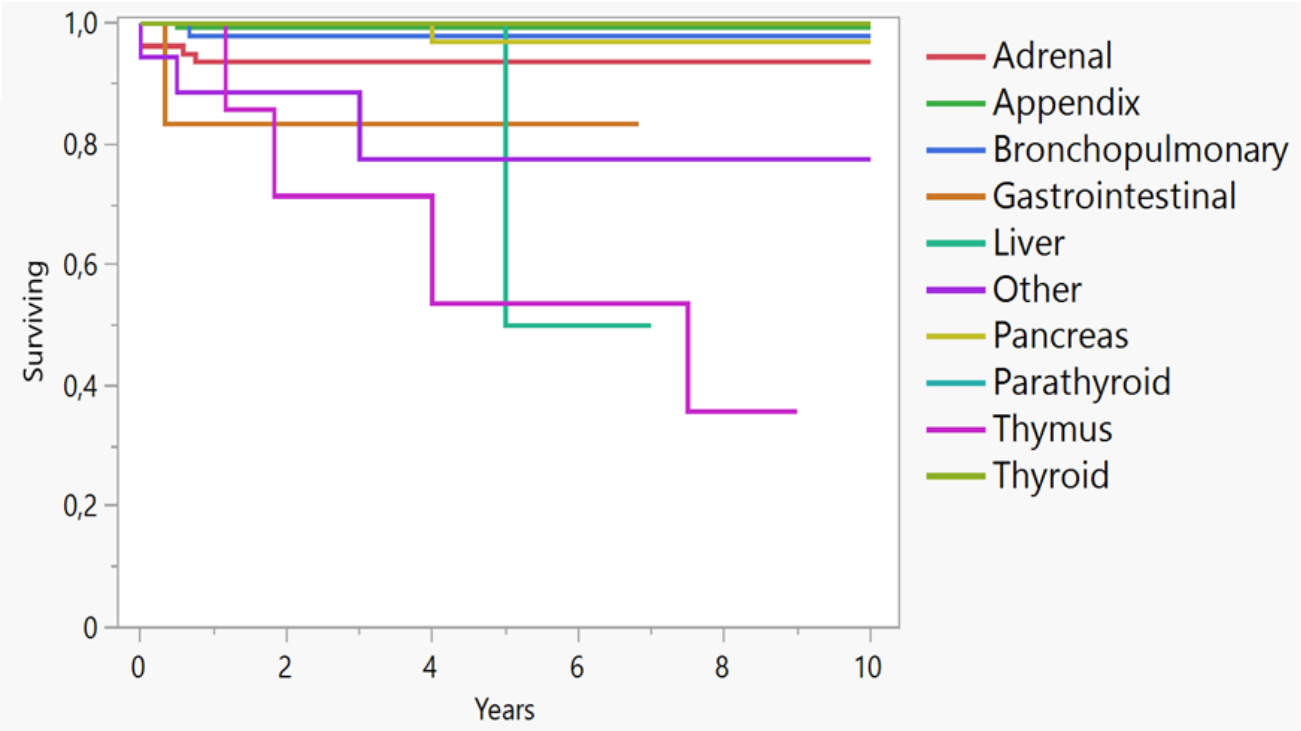

Figure 2. Kaplan-Meier survival analysis for different tumor sites in pediatric NET.

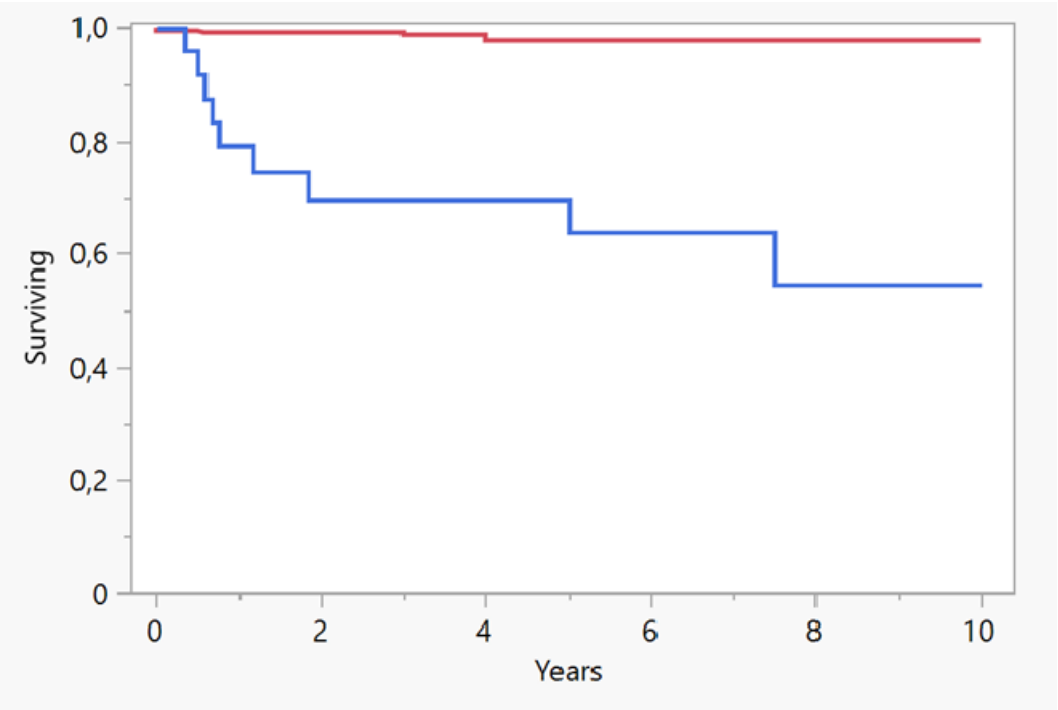

Figure 3. Kaplan-Meier analysis for survival with localized (red) vs. metastatic (blue) NET.

References

[1] Farooqui ZA, Chauhan A. Neuroendocrine Tumors in Pediatrics. *Glob Pediatr Health* 2019;6:2333794X19862712. doi: 10.1177/2333794X19862712

[2] Navalkele P, O'Dorisio MS, O'Dorisio TM, et al. Incidence, survival, and prevalence of neuroendocrine tumors versus neuroblastoma in children and young adults: nine standard SEER registries, 1975-2006. *Pediatr Blood Cancer* 2011;56(1):50–7. doi: 10.1002/pbc.22559

[3] Dasari A, Shen C, Halperin D, et al. Trends in the Incidence, Prevalence, and Survival Outcomes in Patients With Neuroendocrine Tumors in the United States. *JAMA Oncol* 2017;3(10):1335–42. doi: 10.1001/jamaoncol.2017.0589

[4] Ankerstjerne MP, Giovannoni S, Christensen LG, et al. Pediatric Neuroendocrine Tumors in Denmark: Incidence, Management, and Outcome From 1995 to 2020. *Pediatr Blood Cancer* 2025;72(2):e31420. doi: 10.1002/pbc.31420

[5] Kulkarni KP, Sergi C. Appendix carcinoids in childhood: Long-term experience at a single institution in Western Canada and systematic review. *Pediatrics International* 2013;55(2):157–62. doi: 10.1111/ped.12047

[6] Howell DL, O'Dorisio MS. Management of neuroendocrine tumors in children, adolescents, and young adults. *J Pediatr Hematol Oncol* 2012;34 Suppl 2:S64–8. doi: 10.1097/MPH.0b013e31824e3885

[7] Kulke MH, Benson AB, 3rd, Bergsland E, et al. Neuroendocrine tumors. *J Natl Compr Canc Netw* 2012;10(6):724–64. doi: 10.6004/jnccn.2012.0075

[8] Virgone C, Roganovic J, Rindi G, et al. Appendiceal neuroendocrine tumors in children and adolescents: The European Cooperative Study Group for Pediatric Rare Tumors (EXPeRT) diagnostic and therapeutic recommendations. *Surgery* 2025;184:109451. doi: 10.1016/j.surg.2025.109451

[9] Abele M, Kunstreich M, Lessel L, et al. Bronchial carcinoid tumors in children and adolescents – A report and management considerations from the German MET studies. *Lung Cancer* 2023;183. doi: 10.1016/j.lungcan.2023.107320

[10] Akova F, Aydin E, Nur Eray Y, et al. Long-term outcomes in pediatric appendiceal carcinoids: Turkey experience. *Eur J Pediatr* 2018;177(12):1845–50. doi: 10.1007/s00431-018-3258-z

[11] Bartsch DK, Albers M, Knoop R, et al. Enucleation and limited pancreatic resection provide long-term cure for insulinoma in multiple endocrine neoplasia type 1. *Neuroendocrinology* 2013;98(4):290–8. doi: 10.1159/000357779

[12] Baykara AS, Bildirici Y. Clinico-Pathological Characteristics and Long-Term Outcomes of Incidental Appendiceal Carcinoid Tumors in Children. *Iranian Journal of Pediatrics* 2023;33(6). doi: 10.5812/ijp-141027

[13] Bolasco G, Capriati T, Grimaldi C, et al. Long-term outcome of pancreatic function following oncological surgery in children: Institutional experience and review of the literature. *World J Clin Cases* 2021;9(25):7340–9. doi: 10.12998/wjcc.v9.i25.7340

[14] Boston CH, Phan A, Munsell MF, et al. A Comparison Between Appendiceal and Nonappendiceal Neuroendocrine Tumors in Children and Young Adults: A Single-institution Experience. *J Pediatr Hematol Oncol* 2015;37(6):438–42. doi: 10.1097/MPH.0000000000000350

[15] Brauckhoff M, Machens A, Lorenz K, et al. Surgical curability of medullary thyroid cancer in multiple endocrine neoplasia 2B: a changing perspective. *Ann Surg* 2014;259(4):800–6. doi: 10.1097/SLA.0b013e3182a6f43a
[16] Broaddus RR, Herzog CE, Hicks MJ. Neuroendocrine tumors (carcinoid and neuroendocrine carcinoma) presenting at extra-appendiceal sites in childhood and adolescence. *Archives of Pathology and Laboratory Medicine* 2003;127(9):1200–3. doi: 10.5858/2003-127-1200-ntcanc
[17] Bussieres V, Roy S, Deladoey J, et al. Prophylactic thyroidectomies in MEN2 syndrome: Management and outcomes. *J Pediatr Surg* 2018;53(2):283–5. doi: 10.1016/j.jpedsurg.2017.11.015
[18] Çetin SK, Şıklar Z, Aycan Z, et al. Clinical Profile of Parathyroid Adenoma in Children and Adolescents: A Single-Center Experience. *Turkish Archives of Pediatrics* 2023;58(1):56–61. doi: 10.5152/TurkArchPediatr.2022.22180
[19] Degnan AJ, Tocchio S, Kurtom W, et al. Pediatric neuroendocrine carcinoid tumors: Management, pathology, and imaging findings in a pediatric referral center. *Pediatr Blood Cancer* 2017;64(9). doi: 10.1002/pbc.26477
[20] Eren E, Saglam H, Caliskan Y, et al. Pediatric patients with pheochromocytoma: Experience of a tertiary health center. *Pediatrics International* 2015;57(5):875–9. doi: 10.1111/ped.12664
[21] Estrella JS, Li L, Rashid A, et al. Solid pseudopapillary neoplasm of the pancreas: clinicopathologic and survival analyses of 64 cases from a single institution. *Am J Surg Pathol* 2014;38(2):147–57. doi: 10.1097/PAS.0000000000000141
[22] Fauroux B, Aynie V, Larroquet M, et al. Carcinoid and mucoepidermoid bronchial tumours in children. *European Journal of Pediatrics* 2005;164(12):748–52. doi: 10.1007/s00431-005-1740-x
[23] Fernández KS, Aldrink JH, Ranalli M, et al. Carcinoid tumors in children and adolescents: Risk for second malignancies. *Journal of Pediatric Hematology/Oncology* 2015;37(2):150–3. doi: 10.1097/MPH.0000000000000280
[24] Henderson L, Fehily C, Folaranmi S, et al. Management and outcome of neuroendocrine tumours of the appendix-a two centre UK experience. *J Pediatr Surg* 2014;49(10):1513–7. doi: 10.1016/j.jpedsurg.2014.05.019
[25] Jellins T, Hill M, Prager JD, et al. Pediatric head and neck manifestations associated with multiple endocrine neoplasia syndromes. *International Journal of Pediatric Otorhinolaryngology* 2023;173. doi: 10.1016/j.ijporl.2023.111703
[26] Karageorgiadis AS, Papadakis GZ, Biro J, et al. Ectopic adrenocorticotropic hormone and corticotropinreleasing hormone co secreting tumors in children and adolescents causing cushing syndrome: A diagnostic dilemma and how to solve it. *Journal of Clinical Endocrinology and Metabolism* 2015;100(1):141–8. doi: 10.1210/jc.20142945
[27] Kartal İ. Childhood neuroendocrine tumors of the digestive system: A single center experience. *Medicine (United States)* 2022;101(6):E28795. doi: 10.1097/MD.0000000000028795
[28] Kim D, Yang HB, Kim HY. Malignant pancreatic tumor other than solid pseudopapillary tumor in pediatric patients A single-center experience. *Medicine (United States)* 2021;100(50):E27967. doi: 10.1097/MD.0000000000027967
[29] Koc G, Sugimoto S, Kuperman R, et al. Pancreatic tumors in children and young adults with tuberous sclerosis complex. *Pediatr Radiol* 2017;47(1):39–45. doi: 10.1007/s00247-016-3701-0
[30] Kuhlen M, Pamporaki C, Kunstreich M, et al. Adrenocortical Tumors and Pheochromocytoma/Paraganglioma Initially Mistaken as Neuroblastoma—Experiences

From the GPOH-MET Registry. *Frontiers in Endocrinology* 2022;13. doi: 10.3389/fendo.2022.918435
[31] Lee PDK, Winter RJ, Green OC. Virilizing adrenocortical tumors in childhood: Eight cases and a review of the literature. *Pediatrics* 1985;76(3):437–44. doi:
[32] Marchegiani G, Crippa S, Malleo G, et al. Surgical treatment of pancreatic tumors in childhood and adolescence: uncommon neoplasms with favorable outcome. *Pancreatology* 2011;11(4):383–9. doi: 10.1159/000330212
[33] Mastrangelo S, Attina G, Rindi G, et al. Characteristics and Management of Children with Appendiceal Neuroendocrine Neoplasms: A Single-Center Study. *Cancers (Basel)* 2024;16(20). doi: 10.3390/cancers16203440
[34] Melikyan M, Gubaeva D, Shadrina A, et al. Insulinoma in childhood: a retrospective review of 22 patients from one referral centre. *Frontiers in Endocrinology* 2023;14. doi: 10.3389/fendo.2023.1127173
[35] Mitra AP, Vasquez E, Kokorowski P, et al. Robotic adrenalectomy in the pediatric population: Initial experience case series from a tertiary center. *BMC Urology* 2020;20(1). doi: 10.1186/s12894-020-00727-x
[36] Mora Fritis C, Ruiz-Tagle PG, Vuletin Solis JF, et al. Adrenal tumors in pediatric patients treated with minimally invasive surgery. *Andes Pediatrica* 2024;95(5):613–9. doi: 10.32641/andespediatr.v95i5.5157
[37] More J, Young J, Reznik Y, et al. Ectopic ACTH syndrome in children and adolescents. *J Clin Endocrinol Metab* 2011;96(5):1213–22. doi: 10.1210/jc.2010-2276
[38] Mowrey K, Northrup H, Rougeau P, et al. Frequency, Progression, and Current Management: Report of 16 New Cases of Nonfunctional Pancreatic Neuroendocrine Tumors in Tuberous Sclerosis Complex and Comparison With Previous Reports. *Front Neurol* 2021;12:627672. doi: 10.3389/fneur.2021.627672
[39] Neary NM, Lopez-Chavez A, Abel BS, et al. Neuroendocrine ACTH-producing tumor of the thymus--experience with 12 patients over 25 years. *J Clin Endocrinol Metab* 2012;97(7):2223–30. doi: 10.1210/jc.2011-3355
[40] Neves GR, Chapchap P, Sredni ST, et al. Childhood carcinoid tumors: Description of a case series in a Brazilian cancer center. *Sao Paulo Medical Journal* 2006;124(1):21–5. doi: 10.1590/S1516-31802006000100005
[41] Oegonomopoulos CT. Argentaffin cell tumours (cftrcinoid.) of the appendix in children. *Pediatrics* 1961;27(1):134–9. doi:
[42] Osman Y, Hussein N, Sarhan O, et al. Surgical analysis of pediatric and adolescent sporadic pheochromocytoma: Single center experience. *International Urology and Nephrology* 2011;43(4):1019–24. doi: 10.1007/s11255-011-9959-0
[43] Park H, Kim MS, Lee J, et al. Clinical Presentation and Treatment Outcomes of Children and Adolescents With Pheochromocytoma and Paraganglioma in a Single Center in Korea. *Front Endocrinol (Lausanne)* 2020;11:610746. doi: 10.3389/fendo.2020.610746
[44] Perel Y, Schlumberger M, Marguerite G, et al. Pheochromocytoma and paraganglioma in children: a report of 24 cases of the French Society of Pediatric Oncology. *Pediatr Hematol Oncol* 1997;14(5):413–22. doi: 10.3109/08880019709028771
[45] Perez-Albert P, de Rojas T, Lendinez MA, et al. Management and outcome of children with neuroendocrine tumors of the appendix in Spain: Is there room for improvement? *Clin Transl Oncol* 2017;19(9):1168–72. doi: 10.1007/s12094-017-1653-y
[46] Potter SL, Haduong J, Okcu F, et al. Pediatric Bronchial Carcinoid Tumors: A Case Series and Review of the Literature. *Journal of Pediatric Hematology/Oncology* 2019;41(1):67–70. doi: 10.1097/MPH.0000000000001100

[47] Rizzardi G, Marulli G, Calabrese F, et al. Bronchial carcinoid tumours in children: surgical treatment and outcome in a single institution. *Eur J Pediatr Surg* 2009;19(4):228–31. doi: 10.1055/s-0029-1202857
[48] Shariq OA, Lines KE, English KA, et al. Multiple endocrine neoplasia type 1 in children and adolescents: Clinical features and treatment outcomes. *Surgery* 2022;171(1):77–87. doi: 10.1016/j.surg.2021.04.041
[49] Spunt SL, Pratt CB, Rao BN, et al. Childhood carcinoid tumors: The St Jude Children's Research Hospital experience. *Journal of Pediatric Surgery* 2000;35(9):1282–6. doi: 10.1053/jpsu.2000.9297
[50] Stackpole RH, Melicow MM. PHEOCHROMOCYTOMA in CHILDREN. REPORT of 9 CASES and REVIEW of the FIRST 100 PUBLISHED CASES with FOLLOW-UP STUDIES. *Journal of Pediatrics* 1963;63(2):315–30. doi: 10.1016/S0022-3476(63)80345-5
[51] Techavichit P, Hicks MJ, López-Terrada DH, et al. Mucoepidermoid Carcinoma in Children: A Single Institutional Experience. *Pediatric Blood and Cancer* 2016;63(1):27–31. doi: 10.1002/pbc.25681
[52] Tian F, Zhao J, Ding D, et al. Clinicopathological Features of Pediatric Insulinoma: A Single-Centre Study. *Br J Hosp Med (Lond)* 2024;85(7):1–13. doi: 10.12968/hmed.2024.0259
[53] Tonelli F, Giudici F, Marcucci T, et al. Surgery in MEN 2A Patients Older Than 5 Years with Micro-MTC: Outcome at Long-term Follow-up. *Otolaryngol Head Neck Surg* 2016;155(5):787–9. doi: 10.1177/0194599816654856
[54] Venara M, Sanchez Marull R, Bergada I, et al. Functional adrenal cortical tumors in childhood: A study of ploidy, p53- protein and nucleolar organizer regions (AgNORs) as prognostic markers. *Journal of Pediatric Endocrinology and Metabolism* 1998;11(5):597–605. doi: 10.1515/JPEM.1998.11.5.597
[55] Virgone C, Ferrari A, Chiaravalli S, et al. Extra-appendicular neuroendocrine tumors: A report from the TREP project (2000-2020). *Pediatr Blood Cancer* 2021;68(4):e28880. doi: 10.1002/pbc.28880
[56] Yıldırım ÜM, Koca D, Kebudi R. Gastroenteropancreatic neuroendocrine tumors in children and adolescents. *Turkish Journal of Pediatrics* 2024;66(3):332–9. doi: 10.24953/turkjpediatr.2024.4526
[57] Diets IJ, Nagtegaal ID, Loeffen J, et al. Childhood neuroendocrine tumours: a descriptive study revealing clues for genetic predisposition. *Br J Cancer* 2017;116(2):163–8. doi: 10.1038/bjc.2016.408
[58] Ströbel P, Zettl A, Shilo K, et al. Tumor genetics and survival of thymic neuroendocrine neoplasms: a multi-institutional clinicopathologic study. *Genes Chromosomes Cancer* 2014;53(9):738–49. doi: 10.1002/gcc.22183
[59] Li YF, Zhang QQ, Wang WL. Clinicopathological Characteristics and Survival Outcomes of Primary Hepatic Neuroendocrine Tumor: A Surveillance, Epidemiology, and End Results (SEER) Population-Based Study. *Med Sci Monit* 2020;26:e923375. doi: 10.12659/MSM.923375
[60] Halfdanarson TR, Rabe KG, Rubin J, et al. Pancreatic neuroendocrine tumors (PNETs): incidence, prognosis and recent trend toward improved survival. *Ann Oncol* 2008;19(10):1727–33. doi: 10.1093/annonc/mdn351
[61] Jensen SLT, Giovannoni S, Ankerstjerne MP, et al. Surgical Management of Paediatric Appendiceal Neuroendocrine Tumors: A 26-year Danish Nationwide retrospective cohort study. *J Pediatr Surg* 2025:162506. doi: 10.1016/j.jpedsurg.2025.162506

[62] Raikot SR, Potter DD, Jr., Day CN, et al. Appendectomy vs Right Hemicolectomy for Pediatric Neuroendocrine Tumor of the Appendix in a National Cohort: A Call to Further Decrease Colectomy. *J Am Coll Surg* 2025. doi: 10.1097/XCS.0000000000001435
[63] de Lambert G, Lardy H, Martelli H, et al. Surgical Management of Neuroendocrine Tumors of the Appendix in Children and Adolescents: A Retrospective French Multicenter Study of 114 Cases. *Pediatr Blood Cancer* 2016;63(4):598–603. doi: 10.1002/pbc.25823