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Review Article

Anesthetic management of patients with carcinoid syndrome and carcinoid heart disease: A systematic review

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Abstract

Background (purpose): Surgery on patients with Carcinoid Syndrome (CS) and Carcinoid Heart Disease (CHD) is a challenge for anesthesiologists due to the high risk of developing Carcinoid Crisis (CC). The purpose of the study is to assess whether or not the use of octreotide as prophylaxis in the perioperative environment would decrease the incidence of CC (PEAK METHOD). We also try to identify CC's precipitating factors.

Material and methods (source): Research upon octreotide efficacy on CC prophylaxis was made on PubMed, Google Scholar, Cochrane, and web of science (WOS), from January 2010 to February 2021. We carried out a retrospective qualitative Systematic Review, which was developed in accordance with the PRISMA statement.

Results (principal findings): Eleven articles were included in the study, five of them are retrospective studies, one is a prospective study, one is a prospective case series, two are retrospective case series, one is a meta-analysis of retrospective studies, and one is a cohort study. 5 of them are retrospective studies, 1 is a prospective study, 1 is a prospective case series and finally, 1 is a meta-analysis on retrospective studies. According to Massimino, et al. 2013; Guo, et al. 2014, Condron, et al. 2016 and Condron, et al. 2019, prophylaxis with octreotide is insufficient, it does not prevent and is inefficient in preventing CC. Tapia Rico et al confirm that due to the use of octreotide as prophylaxis, 1 patient experienced CC and 6 symptoms of CS. Fouche, et al. conclude that with prophylaxis, intraoperative carcinoid syndrome (ioCS) was mostly hypertensive. For the retrospective review that Kinney, et al. carried out, it was found that 169 patients did not experience CC. In the review carried out by Woltering, et al. it was found that out of 179 cytoreductive surgeries, prophylaxis with octreotide decreased the incidence of CC, they registered only 6 cases of CC (3,4%).

Discussions and conclusions: Although octreotide constitutes the cornerstone for the prevention and treatment of CC, the current data does not support the idea that it is totally effective in preventing it.

Introduction

Neuroendocrine neoplasms (NEN) are tumors derived from the neuroectoderm (from the neural crest) [1,2]. OMS classifies every neuroendocrine cancer as neuroendocrine neoplasms (NEN) that can divide into well-differentiated neuroendocrine carcinomas (NET) [1-4] and poorly differentiated neuroendocrine carcinomas (NEC), later called mixed neuroendocrine neoplasia (MiNEC) [5,6].

Most NEN is found in the gastrointestinal tract (55%) or in the bronchopulmonary tract (25%) [2,5,7,8]. NEN in the

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small intestine metastasize more frequently [5] and are the main cause of CS [9]. Up to 30-40% of the patients with NEN experience CS [10].

NEN's incidence is rising all over the world due to the improvement of imaging techniques. It affects 1.2-35/100.000 people each year [2,4,5,7,11]. It is more frequent in African-American women [5].

They can synthesize, store and secrete up to 40 vasoactive substances like serotonin, main substance, (diarrhea, cardiac valve lesions), tachykinins (substance P), histamine, and kallikreins (skin redness), prostaglandins (PG), catecholamines, and motilin to the bloodstream [1]. In healthy individuals, serotonin is metabolized mainly to 5-hidroxiindolacetic acid. When there is liver metastasis, liver degradation is blocked and the substances reach the systemic circulation, inferior vena cava, and lastly, the right side of the heart, developing CS as a result (rush, diarrhea, and bronchospasm) [2,12]. The exceptions to this pathophysiological pathway are ovarian carcinoids that drain directly into the systemic circulation or very rare cases of extensive metastases in the retroperitoneal lymph nodes (<1%), forcing thoracic duct drainage [1,2,6,8,11-13].

Most episodes of CS occur spontaneously but can be provoked by certain foods, alcohol, defecating, emotional stress, liver palpation, and anesthesia [2].

20 to 50% of the individuals with CS were diagnosed with carcinoid heart disease (CHD) [2,7,13].

In medical treatment, there are two somatostatin analogs (SSTA) available, octreotide and lanreotide (approximately 80% of neuroendocrine tumors have somatostatin receptors). The use of somatostatin analogs inhibits serotonin and vasoactive intestinal peptide secretion, leading to the control of CS symptoms such as diarrhea and hot flushes. It also helps stabilize blood pressure (BP). Many studies have shown that octreotide and lanreotide can also inhibit the proliferation of tumor cells [12].

Carcinoid heart disease

Carcinoid Heart Disease (CHD) (Hedinger's Syndrome) is characterized by fibrous tissue deposits, such as plaques, pathognomonic in heart valves and in the endocardium, mainly on the right side of the heart (tricuspid regurgitation, pulmonary stenosis) [11]. Prolonged exposure to high serotonin blood concentrations is a crucial factor [2,4]. The stimulation of serotonin receptors (5HT 2B) increases the cardiomyocyte and fibroblasts' mitogenic activity. Levels of 5-HIIA above 300 umol/24 hours, more than 3 redness episodes per day, and the N-terminal pro-brain natriuretic peptide (NT-proBNP) have been considered very useful as a tool for the diagnosis, development, or progression of CHD in patients with CS [2,14,15].

Carcinoid crisis

CC is an acute and potentially fatal CS complication caused by the sudden release of 5-HT and other vasoactive peptides such as tachykinins, histamine, kallikrein, prostaglandins, motilin, or catecholamines, by carcinoid tumor cells [1]. This causes intensive blushing, bronchospasms, deep hypotension, hemodynamic instability, and arrhythmias. On the other hand, there is no clear consensus on its precise definition [1,2,8,12,16]. Retrospective, prospective, and case series studies use different definitions [17-24]. (Table 1 definition). In a perioperative context, the retrospective series notified a CC incidence of 30% in patients with CS.

It can occur spontaneously after medication intake, alcohol, abdominal palpation, induced anesthesia, surgery (tumor manipulation), tumor necrosis due to chemotherapy, hepatic artery ligature or embolization, intra-arterial therapy, (hepatic artery embolization, chemoembolization, and radio-embolization), bronchoscopy, echography, and mammography [16,18,21-23,25-41].

Some studies have identified a group of patients at high risk for developing intraoperative CC [20,42]. These patients include those with a significant tumor burden, liver metastases [18,20] coronary heart disease, elevated levels of 5-HIAA in urine [20,22] and chromogranin A, presence of previous uncontrolled CS (although patients without CS or liver metastases may develop CC) [20,42] duration of surgery and advanced age [20] (See perioperative data in Table 2).

Histamine-releasing drugs such as sympathomimetic bronchodilators are also precipitating factors, although Limbach, et al. 2019 in their retrospective study concluded that β-agonists are not associated with secondary CC [43]. See precipitating factors [7,18-24,43-45] (Table 3).

The presence of coronary heart disease and elevated levels of 5-HIAA represent predictors of an emerging CC. Patients with a large tumor burden, elevated chromogranin A levels, or elevated urine 5-HIAA levels are more likely to experience a CC episode during surgery; however, not all of these risks have been systematically confirmed [9]. In these, perioperative prophylactic octreotide will be especially considered; calcium and catecholamines cause the release of tumor mediators and worsen the syndrome [5,9,22,30].

The criteria for its definition are not well established, so its actual incidence is unknown [28]. There is no standard definition of CC [17-24,32], Table 1) being used to describe a range of conditions. This makes it difficult to draw conclusions regarding the incidence and severity of CC episodes, and therefore to propose prophylactic guidelines and treatment protocols.

CC prevention

Perioperative management: We must improve and stabilize the patient with symptoms of CS. Premedication with benzodiazepines and antihistamines can be useful to reduce anxiety, but their administration is controversial, since histamine release can occur, especially in gastric and bronchial carcinoids. Although corticosteroids may not prevent anaphylactic shock, they can reduce episodes caused by nonspecific histamine release [28].

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Table 1: Definition Of CC.

Fujie 2010 [32]	Life-threatening hypotension, with arrhythmias, bronchospasm, facial rash, edema, metabolic acidosis, confusion, coma, and death.
Massimino 2013 [18]	CC does not have a strict definition, it is considered as the sudden onset of life-threatening features of CS, rash, diarrhea, bronchospasm, tachycardia, bradycardia, HT, hypotension, and fever. That can cause vasomotor collapse and death. Intraoperative complications are defined as prolonged hypotension (SAT≤80mmHg>10min) or hemodynamic instability (hypotension, hypertension, or tachycardia) not attributed to acute blood loss or obvious causes treated by the anesthetist or by the surgeon.
Condron 2015 [20]	Significant hemodynamic instability is not attributed to compression of the inferior vena cava, blood loss, SBP (≤80 o > de 180mmHg≥10 minutes, HR >120 bpm with organ dysfunction (ventricular arrhythmias or bronchospasm).
Woltering 2016 [21]	CC is a potentially life-threatening exacerbation of CS characterized by rash, bronchospasm, tachycardia, and wide BP fluctuations (SBP <80mmHg ≥10 min); hemodynamic instability not explained by blood loss or volume status.
Kinney 2018 [22]	Sudden or abrupt onset of at least two of the following: Rash or hives are not explained by an allergic reaction. Bronchospasm or treatment with bronchodilators (Albuterol) Hypotension, SBP <80 mmHg for ≥10 min not explained by volume status of bleeding and treated with vasopressors. Arrhythmia is not explained by volume status or bleeding Tachycardia ≥120 bpm
Fouche 2018	Life-threatening ioCS, refractory to octreotide boluses, including hemodynamic instability, cardiac arrhythmias, cardiogenic shock, and bronchodilators - ioCS is so highly probable if there are changes in BP ≥40% or rapid HR in less than 5 min that are not explained by anesthetic/surgical management and that return ≥20% after the IV bolus of octreotide - ioCS is probable: rapid onset in 5-10 minutes and/or hemodynamic changes 20-40% and does not revert ≥ 20% with octreotide - ioCS is suspicious: ioCS that is detected by an injection of octreotide recorded in the anesthesia registry is neither highly probable nor probable.
Otros: Modlin 2010 Guo 2014 [19] Tapia Rico 2018 [24]	CC is an exacerbation of CS and the main symptoms include rash, diarrhea, hemodynamic instability (hypotension and more rarely hypertension), bronchospasm, and mental disturbances. CC is a life-threatening syndrome of Neuroendocrine Tumors (NETs) characterized by dramatic fluctuations in BP, arrhythmias, and bronchospasm.

CC: Carcinoid Crisis; ioCS: intraoperative Carcinoid Syndrome

Intraoperative hypotension, hypertension, and hypercapnia should be avoided [2]. Different methods have been proposed for the prophylactic administration of SSTA. There is no international consensus on the best regimen or form of administration of octreotide, subcutaneously (sb), or in continuous intravenous (IV) infusion. Several protocols have been devised, from the Mount Sinai [8], of the European Neuroendocrine Tumor Society (ENETS) [9] the American Neuroendocrine Tumor Society (NANETS) [46] or the UK and Ireland Neuroendocrine Tumour Society NETS [47] However, the efficacy of using somatostatin analogs has not been fully evaluated and the programs are generally based on the personal experience of the author. Most of them label the prophylactic use of octreotide as the fundamental measure to try to prevent CHD [2]

The prophylactic administration of octreotide (300-500 µg sb or iv), prior to the resection of liver metastases, (levels of evidence Grade 1B), as well as its prophylactic use for patients with CS and extensive tumor before embolization of the hepatic artery (Grade 1B) decreases the incidence of CC. Some recommend prophylactic octreotide for CS patients before surgery, while others advocate it for all NET patients scheduled for surgical resection. For those whose symptoms cannot be adequately relieved by medical therapy, close monitoring of the CC is crucial to avoid life-threatening events [16].

The Mont Sinai protocol begins with a preventive infusion of 50-100 µg /hour at least 12 hours before proceeding and 48 hours postoperatively; infusion maximized to 300 µg/h if it is necessary.

During induction, a bolus of 50-100 µg can be administered routinely.

Transthoracic echocardiography can be performed 48 hours before surgery. On the morning of surgery, the patient can be premedicated with 500 µg of octreotide (sb or iv) and in both 10 mg of dexchlorpheniramine, 200 mg of hydrocortisone, and 150 mg of iv ranitidine y 2 mg of midazolam in the operating room. After standard monitoring plus invasive blood pressure with local anesthesia, induction can be done with TIVA, fentanyl, propofol, and cis-atracurium (we must avoid Morphine, atracurium that release histamine, and Suxamethonium that produces fasciculations).

Anesthesia maintained with propofol 3-6 mg/kg/hour, fentanyl 150ug, and cis-atracurium boluses [2]. Remifentanil (0.05–0.2 µg kg^{-1} min^{1}) in optimizing intubating conditions,

Two peripheral lines of large caliber 16-G and 18-G and the central venous line must be inserted. CC considers phenylephrine and epinephrine in RV dysfunction [8].

Laparotomy with epidural catheter placement may be beneficial as long as we avoid hypotension associated with its use [27].

We benefit from hemodynamic monitoring and the Bispectral Index (BIS) (BIS, Covidien, IIc, Mansfield, USA). Thermal covers were also used.

Methods

We conducted and presented this systematic review using the Preferred Reporting Items for Systematic Review and Meta-Analysis statement (PRISMA-ScR) (Figure 1).

Eligibility criteria

The studies chosen included patients with a history of

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Table 2: Datos Perioperatorios.

	Duration of the anesthesi a (min)	Intraopera tive carcinoid crisis(CC)	Duration of CC	ASA	Location of primary tumor	Metastasis	Age at the time of the surgery	5- HIAA (In urine in 24 H) N: (0-41,84µmol/d)	Chromogran in A N:(≤93µg/L)	CS	CHD	CC PRECIPITA TING FACTORS	PRO PHY LAX IS
Massimino 2013 [18] Retrospective Study		21/87 p 0,77 (24,1%)with proph. 2/10(20.0) no prophylaxis 97 patients		ASA II.24 (24,7%)AS A III 69(72,9%)A SA IV 2 (2,1%)	Small Intestine 65(67,0) Appendix.....7(7,2) Colon/Rectum.....5(5,2) Others.....7(7,2) Unknown.....13(18,4)	Hepatic.....75(77,3) Mesenteric..... 46(47,4) Others.....27(27, 8)	Mean age 59,3 years M 41 F 56			-Patient with CS :57(58,8) N:97 -Patient without CS: 47	-Patients with CHD..2(2,1)	SEE TABLE 3	YES
Guo 2014 [19] retrospective Studies Metaanalisis		53 cases of CC 28 patients			Small Intestine Respiratory system		60a 17V, 11M				18,9%	SEE TABLE 3	YES
Condron 2016 [20] Prospective Case series	-NO events 298 min (203-365) -With events 370(278454). -Combined 318min(227 -382 mean or frequency	45/150 surgeries (30%) (127 patients/15 0 surgeries)	8,7 min	Most of them were ASA III	Small intestine	Hepatic.....71 Mesenteric...68 Others.....35	-NO events 60a(52,67) -With events 61a (54,66) -Combined 61a(54,66)	Mean in patients with CS 43µmol/d Mean in patients without CS 17µmol/d	Mean 2413(µg/L) Median 113(µg/L)	-No previous symptoms. NO events...32%(34) -No previous symptoms. NO events... ...11%(5) -With previous symptoms. NO events... ...68%(71) -With previous symptoms. NO events...89%(40)	-NO CHD, no intraoperative events...96%(101) -NO CHD, with intraoperative events...98%(44) -CHD patients. No intraoperative events...4%(4) -CHD patients, with intraoperative events ...2%(1)	SEE TABLE 3	YES
Woltering 2016 [21] Retrospective Review	378min± SD(T°me dio±S)	6/179 surgeries (3,4%)		M69(46%) F81(54%)	Ileum...73(49) Terminal ileum.36(24 Jejunum...2(1) Small intestine 39 (26). Not specified		Mean age 59±10ª Median 59y(31-80ª)			-Pat. with CS 150(85%)		SEE TABLE 3	YES
Welch 2016 [45] retrospective Review		11 patients 1 CC		ASA 3: 10 ASA 4: 1	RESPIRATORY: 3 SMALL INTESTINE :2 THYMUS 1 UNKNOWN 2	11 BRAIN MTX CARCINOID	Median de 60ª. 45% Male			2 CS		SEE TABLE 3	YES
Tapia rico 2018 [24] Retrospective Case series	RRTP	7 PATIENTS: 1 patient with CC, 6 carcinoid symptoms CC: 3,2-3,5% 7 PREVIOUS CC				3 HEPATIC MTX			High GC in 5 patients	7 CS	1 CHD	SEE TABLE 3	YES

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Fouche 2018 Retrospective Review		81 PATIENTS (42 MALES) 139 ioCS (**highly probable 45**, p 67 y s 27)		ASA I-II: 65 ASA III-IV 16	SMALL INTESTINE	59 HEPATIC MTX 7 EXTRAADBOMINAL MTX		HIGH LEVELS IN 40 PATIENTS		49 PREVIOUS CS	7 PREVIOUS CHD		YES
Kinney 2018 [22] Retrospective Review	294±78m in (mean duration)	0,0%;95% CI 0,0-2,2%		ASAII.70(41,4) ASAIII 96(56,8) ASAIV 3(1,8) Age: Median 60 (51,68) M83(49,1) F86(50,9)A	Small intestine.118(69,8%) Colon/rectum…… 17(10,1%) Bronchus……7(4,1%) Others……6(3,6%) Unknown……21(12,4%)	Hepatic….169(196)	Mean age at time of surgery 60y (IQR 5168)	Median 220 (89,596). (25th75th) 51% patients (87/169) had high preop. 5-HIAA levels 4% (7/169) N	Median 675 µg/L (1821305). (25th75th)	-Patients with CS 130	-Patients with CHD 14 (8,3%)	SEE TABLE 3	YES
Limbach 2019 [43] Retrosopective Review	371,08 VS 382,55 (p0,761)	161 CC; 20,7% (phenylephrine) vs 12,9 % (β agonists) NO MEANING	8,08 min VS 10,7(p 0,257)		SMALL INTESTINE 33 VS 20 (p, 627)	Hepatic 32 vs 19(p0,775 Mesenteric 27vs18 (p0,545) Others 11 vs 10(p0,252)	Age:60,64 vs 62(p 0,572) FEMALE 24 VS 16(P 0,628			30 vs 19 (p 0,757)		SEE TABLE 3	YES
Condron 2019 [43] Prospective Study	Mean duration 349 min (range 208-543)	16 CC/46 patients	Mean 8,1 min (317min)		1º hepatic cytoreductive surgery NO CRISIS:25 CRISIS:12 P 0,497 Most frequent primary location: Small intestine: 40 patients(87%)	31 mesenteric metastases. (67%) 9 carcinomatosis(13%)	Crisis: Mean age 63,3 years, 16 M NO crisis: 62,1 years old , 12H. p0,652			NO Crisis: 19SC Crisis: 11SC P 0,713 CS 30pat. (65%)		SEE TABLE 3	YES
Shabtaie 2021 [7] retrospective Review		1 CC/ 17 patients		Mean (62,4+- 9,3 years) 52,9 % Males	Primary location + fr: -Digestive system -Lungs -Ovary	9 patients presented metastatic disease.				3 patients	2 patients	SEE TABLE 3	YES

CC: Carcinoid Crisis; CS: Carcinoid Syndrome; CHD: Carcinoid Heart Disease; H: Female; M: Male MTX: Metastasis

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Table 3: Precipitating factors and prophylaxis.

Author	CC precipitating factors	Prophylaxis pattern
Massimino 2013 [18]	-Hepatic MTX -Functioning (21%) and non-functioning tumors (28%) -Prolonged hypotension, hemodynamic instability. -Anesthetic induction, incision, QCA manipulation, liver resection, mesenteric mass resection. -Loss of blood with complications 430 ml (170-1000ml) and no complications 200 ml (100-400). -Blood transfusion -Emotional stress -Catecholamine use -Major and minor QCOs procedures -Arteriography -Epidural catheter placement, not use.	a) Long-term ambulatory octreotide (LAR) in 70 patients b) 87 patients (90%) received preoperative IV boluses of octreotide (100-1000 µg) with a median of 500µg. c) Continuous intraoperative IV infusion of 50 µg /hour of octreotide.
Guo 2014 [19]	-Anesthesia/surgery 33 cases (63.5%) -Interventional therapy 6 cases (11.5%) -Radionuclide therapy 5 (9.6%) -Body examination (Eco. Colonos. 4) (7.7%) -Medication 2 (3.8%) -Biopsy 1 (2%) -Spontaneous 1 (2%)	Variable from LAR, a bolus of 250-1000 µg before invasive procedures (Oberg), to continuous IV of octreotide 50mg/h 12 hours before and up to 48 hours after (Ramage)
Condron 2016 [20]	-Liver MTX -High levels of 5-HIAA -CS but not required for the CC to occur -Increase the duration of anesthesia -Female: There are more complications in females but do not correlate with an increase in CC -Advanced age, higher incidence of complications	a) Preoperative bolus of 500 µg followed by b) continuous IV infusion of 500 µg /hour
Woltering 2016 [21]	-QCO or anesthetic stimulus -Radiologic interventions -CS -Exercise. -Alcohol. -Large intake of foods rich in tyramine	83% of the patients (149/179) were on long-term outpatient LACREOTHYDE (LAR) OR OCTREOTIDE ACETATE. Intravenous infusion of 500 µg / h of octreotide acetate preoperatively, intraoperatively, and postoperatively. 500 µg IV boluses if needed.
Welch 2016 [45]	Physiological stress, exercise, large intake of foods rich in serotonin, physical manipulation of the tumor, spontaneous anesthesia induction	4 patients received somatostatin analogs.
Tapia rico 2018 [24]	PRRT	Long-acting analogs were stopped 1 month earlier; octreotide 100µg/hour up to 24 hours prior to the procedure.
Fouche 2018	Stress, hypoxemia, hypothermia, hypo or hypertension, pain, induction of anesthesia, tumor manipulation, and pharmacological agents, including anesthetic drugs (vasopressors).	a) Continuous preoperative infusion of 40 or 80 µg/h (if the patient had previous CS, MTX, or CHD) 12-48 hours prior to surgery. b) Continue with continuous IV infusion at doses of 40-80 µg/h during intraoperative and postoperative
Kinney 2018 [22]	-Liver QCA manipulation -Vena cava compression -Intraoperative hemorrhage -Hepatic vascular clamping -Increased 5HIAA (87/169) -Pharmacological agents (anesthetics and Vasopressors).	a) Long-acting (LAR) outpatient monthly injection in 28% of patients (48/169). b) Despite the monthly LAR, 77% (130/169) received 500µg sb preoperatively of octreotide SA. **c)** 23% of patients (39/169) received 500µg of IV octreotide intraoperatively**.**
Limbach 2019 [43]	-Anesthesia/surgery -Vasopressors	A preoperative bolus of 500 µg of iv octreotide, followed by an infusion of 500 µg/ hour iv of octreotide for the duration of the surgery.
Condron 2019 [43]	-Anesthesia/surgery	-LAR -Bolus of 500 µg of octreotide before induction of anesthesia, -Continuous infusion of 500 µg /hour until the end of the surgery.
Shabtaie 2021 [7]	-Anesthesia/catheter ablation -CS active -CHD	Whether CS is active or CHD present, octreotide 2-4 weeks before ablation.

NET with CHD, with or without CS or CHD, scheduled or in an emergency for resection surgery, embolization, RRTP, arteriography, or another type of surgery, who received perioperative prophylaxis with octreotide. We analyze the appearance of CC, and CHD, in the number of patients, sex, and age... according to the definition established by the author.

As inclusion criteria, it was considered that they were fully-text articles, conducted in humans and articles available in English published between 2010-2021, informing the use of the prophylactic value of octreotide in CC.

On the other hand, the following were excluded on the basis of one case: letters to the editor, editorials, conference

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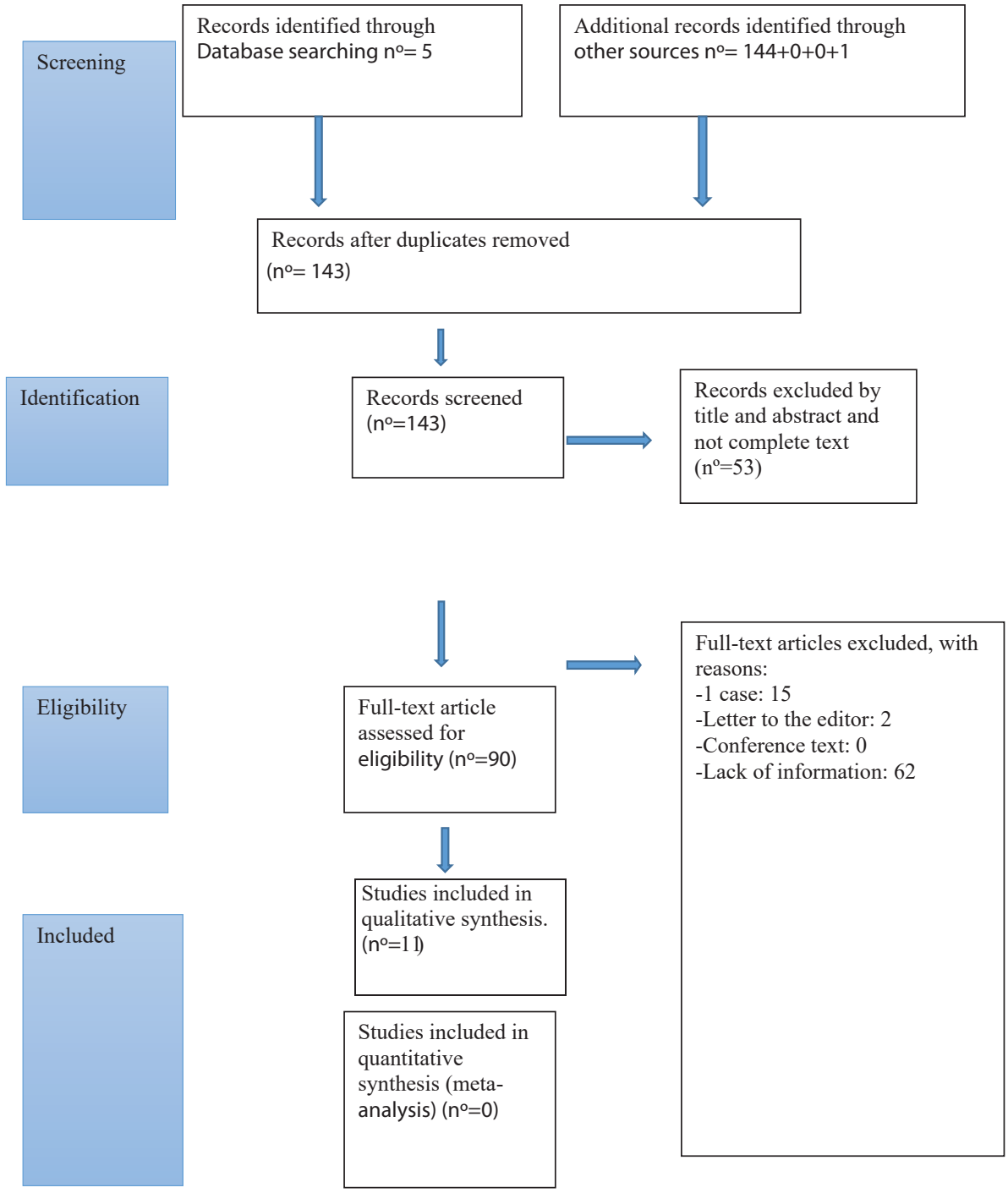

Figure 1: Flow Chart PRISMA 2009.

texts, unavailable full text, and text that, although a study of the prophylactic use of octreotide in CC, did not document it with specific studies. They were excluded because the use of octreotide in the prevention of CC was our first objective; we also wanted to delve into the precipitating factors.

Search strategy

It was carried out using MEDLINE (accessed from PubMed), Google Scholar and the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library, Excerpta Medica (EMBASE), and WOS (web of science). The search strategy was based on the population, intervention, comparator, outcome (PEAK) framework and was designed to find studies and reviews, from the last ten years, related to the usefulness of octreotide in the prevention of CC. The keywords "carcinoid crisis" AND anesthesia AND octreotide AND (prophylaxis or prevention) were used. This search strategy was developed by a biostatistician with experience in systematic reviews.

Two authors independently searched for relevant publications and reviewed the studies identified in the

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bibliography below. The relevant reference lists as well as the articles included in this review were assessed by the two reviewers to identify the articles that fit our inclusion criteria. The two reviewers discussed the obtained results and updated the data continuously. Approval was obtained from COMITÉ DE ÉTICA DE LA INVESTIGACION CON MEDICAMENTOS DEL ÁREA DE SALUD DE SALAMANCA (CEIm Code PI 2018 11 140) dated July 27, 2019, and the patient's informed consent.

Study selection

The two reviewers assessed the eligibility of the articles identified over a period of time from 2010 to 2021. Doubts were resolved by consensus between them.

Data abstraction

From the articles included and always in accordance with the definition of CC given by each author, the following data were obtained:

Type of study, year of publication, age, sex, type of surgery, precipitating factors, octreotide prophylaxis, appearance or not of CC, usefulness or not in preventing CC, the perioperative protocol used, the appearance of CHD. We accompany a scheduled patient for various interventions, with a history of CS, CHD, and previous CC.

Study quality assessment tools were followed for systematic reviews according to the National Heart, Lung, and Blood Institute. The validity of each included study was carried out using nine items for which the affirmative (+), negative (-), or other, including "cannot be determined", "not applicable" and "not reported", (ie, unclear responses) was assigned and rated as good (7-9), fair (4-6), or poor (3 or less) for each individual study [28,48].

Results

Study selection

Our electronic research on Medline identified 5 articles, together with another 145 identified through other sources such as Google Scholar (n=144), The Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library (n = 0), Excerpta Medica (EMBASE) (n = 0) and WOS (web of science n = 1).

After reviewing titles, abstracts, and full texts, 90 articles were included for eligibility; in the end, 11 articles met the inclusion criteria after excluding clinical case reports, letters to the editor, and texts with a lack of information (Figure 1).

Characteristics of the study

Of the included articles, five of them are retrospective studies, one is a prospective study, one is a prospective case series, two are retrospective case series, one is a meta-analysis of retrospective studies, and one is a cohort study. The characteristics of the study, mean age, history of hepatic MTX, CS or CHD, type of procedure used, most frequent primary location, octreotide prophylaxis used, and dose; appearance or not of CC are shown in Table 2. All articles were published between 2010 and 2021.

The selected articles were Massimino et al. [18] 2013; Guo, et al. 2014 [19] Condron, et al. 2016 [20] Woltering, et al. 2016 [21] Welch et al. [45] 2016; Tapia Rico et al. [24] 2018; Fouche, et al. 2018 [23] Kinney, et al. 2018 [22] Limbach, et al. 2019 [43] Condron, et al. 2019 [44] y Shabtaie, et al. 2021 [7]. In them, a large proportion of patients had a history of CS, hepatic MTX, and in some cases CHD. The most common primary site was the small intestine (ID); the most frequent type of procedure was SI resection, followed by hepatic resection, cytoreductive hepatic MTX, and PRRT.

According to Massimino, et al. 2013; [18] Guo, et al. 2014; [19] Condron, et al. 2019, [44] octreotide prophylaxis is insufficient, it does not prevent nor is effective in preventing CC. Tapia Rico, et al. [24] concluded that despite prophylaxis with octreotide, 1 patient had CC and 6 had symptoms of CS. Fouche, et al. [23] concluded that with prophylaxis the IoCS was mainly hypertensive. Kinney, et al. 2018 [22] in their retrospective review with 169 patients did not report any CC. Woltering, et al. [21] in their review of 179 cytoreductive surgeries, affirm that prophylaxis with octreotide does decrease the incidence, documenting only 6 cases (3,4%).

This review has also helped us state that beta-agonists are not associated with secondary CC (Limbach 2019) [43]. In the brain MTX resection by Welch, et al. 2016 [45] only one episode of CC was observed, of course, their retrospective study was only made on 11 patients. Shabtaie, et al. 2021 [7] in another retrospective study made on 17 patients for arrhythmia ablation with a catheter, only reported one CC episode.

Discussion

The efficacy of somatostatin analogs in preventing CC is controversial. The results are contradictory between the different studies. Although current evidence is limited to small series, the use of octreotide infusion has been proposed to prevent intraoperative CC. However, the literature in this regard and recent evidence do not support its efficacy in preventing it. A retrospective study [18] on 97 patients indicated that octreotide LAR and single-dose prophylactic octreotide were not associated with a reduced incidence of perioperative CC.

A recently published retrospective meta-analysis supported these findings, this time with continuous infusion [19]. A prospective study was conducted by Condron 2016 [20] evaluated the preventive use of a 500 µg octreotide perioperative bolus followed by continuous intraoperative infusion at a rate of 500 µg /hour. The seizures occurred with a frequency similar to that of the control of a previous series (30% vs 24%). This author in a subsequent study on 46 patients in 2019 [44] reaffirmed that it was ineffective in preventing CC, as 16 cases of CC were found. Fouche et al. 2018 [23] in their retrospective case series study in 81 patients found 139 ioCS in 45 patients, 45 cases of highly probable ioCS (CC), 67 probable ioCS, and 27 suspicious ioCS.

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On the other hand, Woltering, et al. 2016 [21] in their retrospective study of 179 cytoreductive surgeries only found 6 episodes of CC (3.4%), concluding that the incidence did decrease. Also, Kinney [22] in his retrospective study of 169 patients did not find any CC. Shabtaie, et al. in 20217 in a cohort study of 17 patients for catheter ablation of cardiac arrhythmias, only had 1 case of CC. Welch, et al. 2016 [45] in their retrospective study found only 1 episode of CC out of 11 patients undergoing brain MTX resection.

The ideal prophylactic schedule and dose of octreotide are not clearly established; various guides recommend different protocols. The ENETS guideline recommends a regimen with octreotide 50-100 µg /hour intravenously 12 hours before, up to 48 h after surgery to successfully prevent CC [9]. The North American Society for Neuroendocrine Tumors Guideline (NANETS) advises that routine administration of octreotide does not prevent CC, but recommends an octreotide program of 100-500 µg /hour intraoperatively [44].

In contrast, the UKI NETS guideline provides an extensive schedule on different categories of patients and types of procedures for the dose and coverage period of octreotide. Medical therapy with somatostatin analogs as demonstrated in the PROMID study of octreotide LAR may improve the time to progression [49].

Somatostatin analogs (SSTA) exert their inhibitory effect on the secretion of NETs through 5 subtypes of somatostatin receptors coupled to the G protein, mainly SSTR2 and SSTR5 [17]. The main mechanism is the decrease in c-AMP and intracellular Ca concentration [17]. However, although octreotide has proven value in preventing and treating CC, the current literature is based on small sample size studies and relatively low-quality data. Perhaps this controversy of the results can be explained by the heterogeneity of NETs, perhaps they do not express somatostatin receptors and thus the SSTA cannot act, perhaps octreotide dose is not capable of overcoming the acute discharge of mediators, perhaps the new pasireotide with affinity on SSR1, SSR2, SSR3, and SSR5 if effective in refractory cases to octreotide and lanreotide, perhaps there is a complementary pathway for the release of mediators.

Some studies have identified a group of patients at high risk for developing intraoperative CC [20,42]. These patients include those with a significant tumor burden, liver metastases [18,20] coronary heart disease, elevated levels of 5-HIAA in urine [20,22] and chromogranin A, presence of previous uncontrolled CS (although patients without CS or liver metastases may develop CC) [20,42] duration of surgery and advanced age [20].

The imaging procedure of choice to diagnose neurosarcoidosis (CNS) disease is magnetic resonance imaging contrast-enhanced (MRI); in the presence of CS and advanced age could be a risk factor for CC [50].

Paragangliomas are other rare neuroendocrine tumors: they have the ability to secrete catecholamines. They arise from the extra-adrenal autonomic paraganglia.

Paragangliomas of the head and neck sometimes release catecholamines. Head and neck paragangliomas are rare, accounting for about 0,6% of head and neck tumors. Less than 5% of head and neck paragangliomas secrete catecholamines.

However, most catecholamine-secreting paragangliomas are found in the abdomen and pelvis. Rachel Moor et al describe us as a nonsecretory clival paraganglioma [51].

In addition, the inconsistent use of the term CC and the scarcity of published articles prevent the adaptation of a universally accepted octreotide dosage. This work has its limitations such as the scarcity of quality studies using octreotide in CC prophylaxis. The heterogeneity of the definition of CC given by each author must be recognized, without there being a single accepted definition or prophylaxis protocol.

Conclusion

Most NEN is found in the gastrointestinal tract (55%) They can synthesize, store and secrete up to 40 vasoactive substances like serotonin, (main substance), tachykinins (substance P), histamine, kallikreins, prostaglandins (PG), catecholamines, and motilin to the bloodstream. In healthy individuals, serotonin is metabolized mainly to 5-hidroxiindolacetic acid. When there is liver metastasis, liver degradation is blocked and the substances reach the systemic circulation, developing CS as a result (rush, diarrhea, and bronchospasm).

CC is an acute and potentially fatal CS complication caused by the sudden release of 5-HT and other vasoactive peptides by carcinoid tumor cells. This causes intensive blushing, bronchospasms, deep hypotension, hemodynamic instability, and arrhythmias. On the other hand, there is no clear consensus on its precise definition. Retrospective, prospective, and case series studies use different definitions. In a perioperative context, the retrospective series notified a CC incidence of 30% in patients with CS.

It can occur spontaneously after medication intake, alcohol, abdominal palpation, induced anesthesia, surgery (tumor manipulation), tumor necrosis due to chemotherapy, hepatic artery embolization, bronchoscopy, echography, and mammography, mostly in patients with extensive tumor bulk.

There is no international consensus on the best regimen or form of administration of octreotide, subcutaneously (sb) or in continuous intravenous (iv) infusion. Several protocols have been devised Mount Sinai, NANETS, ENETS, NETS.

The prophylactic administration of octreotide (300-500 µg sb or iv), prior to the resection of liver metastases, (levels of evidence Grade 1B), as well as its prophylactic use for patients with CS and extensive tumor before embolization of the hepatic artery (Grade 1B) decreases the incidence of CC. Some recommend prophylactic octreotide for CS patients before surgery, while others advocate it for all NET patients scheduled for surgical resection. For those whose symptoms cannot be adequately relieved by medical therapy, close monitoring of the CC is crucial to avoid life-threatening events.

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Somatostatin analogs can reduce the risk of developing CHD and possibly inhibit the progression of the existing disease since reduce circulating serotonin levels (periodic echocardiography is recommended and/or monitoring of serum levels of N-terminal brain natriuretic peptide)

Although octreotide is the cornerstone in the prophylaxis and treatment of CC, current studies point to a lack of efficacy in the prevention of CC.

References

1. Clement D, Ramage J, Srirajaskanthan R. Update on Pathophysiology, Treatment, and Complications of Carcinoid Syndrome. J Oncol. 2020 Jan 21;2020:8341426. doi: 10.1155/2020/8341426. PMID: 32322270; PMCID: PMC7160731.

2. Binas D SA, Wulf H, Wiesmann T. Perioperative Management of Patients with Carcinoid Syndrome/Neuroendcrine Neoplasm. . Anästh Intensivmed. 2020; (61):016-24.

3. Boudreaux JP, Klimstra DS, Hassan MM, Woltering EA, Jensen RT, Goldsmith SJ, Nutting C, Bushnell DL, Caplin ME, Yao JC; North American Neuroendocrine Tumor Society (NANETS). The NANETS consensus guideline for the diagnosis and management of neuroendocrine tumors: well-differentiated neuroendocrine tumors of the Jejunum, Ileum, Appendix, and Cecum. Pancreas. 2010 Aug;39(6):753-66. doi: 10.1097/MPA.0b013e3181ebb2a5. PMID: 20664473.

4. Oleinikov K, Korach A, Planer D, Gilon D, Grozinsky-Glasberg S. Update in carcinoid heart disease - the heart of the matter. Rev Endocr Metab Disord. 2021 Sep;22(3):553-561. doi: 10.1007/s11154-020-09624-y. Epub 2021 Jan 14. PMID: 33443717.

5. Ahmed M. Gastrointestinal neuroendocrine tumors in 2020. World J Gastrointest Oncol. 2020 Aug 15;12(8):791-807. doi: 10.4251/wjgo.v12.i8.791. PMID: 32879660; PMCID: PMC7443843.

6. Jin XF, Spampatti MP, Spitzweg C, Auernhammer CJ. Supportive therapy in gastroenteropancreatic neuroendocrine tumors: Often forgotten but important. Rev Endocr Metab Disord. 2018 Jun;19(2):145-158. doi: 10.1007/s11154-018-9443-6. PMID: 29464446.

7. Shabtaie SA, Luis SA, Ward RC, Karki R, Connolly HM, Pellikka PA, Kapa S, Asirvatham SJ, Packer DL, DeSimone CV. Catheter Ablation in Patients With Neuroendocrine (Carcinoid) Tumors and Carcinoid Heart Disease: Outcomes, Peri-Procedural Complications, and Management Strategies. JACC Clin Electrophysiol. 2021 Feb;7(2):151-160. doi: 10.1016/j.jacep.2020.08.009. Epub 2020 Oct 29. PMID: 33602395.

8. Castillo J, Silvay G, Weiner M. Anesthetic Management of Patients With Carcinoid Syndrome and Carcinoid Heart Disease: The Mount Sinai Algorithm. J Cardiothorac Vasc Anesth. 2018 Apr;32(2):1023-1031. doi: 10.1053/j.jvca.2017.11.027. Epub 2017 Nov 20. PMID: 29273478.

9. Kaltsas G, Caplin M, Davies P, Ferone D, Garcia-Carbonero R, Grozinsky-Glasberg S, Hörsch D, Tiensuu Janson E, Kianmanesh R, Kos-Kudla B, Pavel M, Rinke A, Falconi M, de Herder WW; Antibes Consensus Conference participants. ENETS Consensus Guidelines for the Standards of Care in Neuroendocrine Tumors: Pre- and Perioperative Therapy in Patients with Neuroendocrine Tumors. Neuroendocrinology. 2017;105(3):245-254. doi: 10.1159/000461583. Epub 2017 Mar 2. PMID: 28253514; PMCID: PMC5637287.

10. Rubin de Celis Ferrari AC, Glasberg J, Riechelmann RP. Carcinoid syndrome: update on the pathophysiology and treatment. Clinics (Sao Paulo). 2018 Aug 20;73(suppl 1):e490s. doi: 10.6061/clinics/2018/e490s. PMID: 30133565; PMCID: PMC6096975.

11. Gade AK, Olariu E, Douthit NT. Carcinoid Syndrome: A Review. Cureus. 2020 Mar 5;12(3):e7186. doi: 10.7759/cureus.7186. PMID: 32257725; PMCID: PMC7124884.

12. Pandit S, Annamaraju P, Bhusal K. Carcinoid Syndrome. StatPearls. Treasure Island (FL). 2021.

13. Bober B, Saracyn M, Kołodziej M, Kowalski Ł, Deptuła-Krawczyk E, Kapusta W, Kamiński G, Mozenska O, Bil J. Carcinoid Heart Disease: How to Diagnose and Treat in 2020? Clin Med Insights Cardiol. 2020 Oct 27;14:1179546820968101. doi: 10.1177/1179546820968101. PMID: 33192110; PMCID: PMC7597558.

14. Bhattacharyya S, Toumpanakis C, Chilkunda D, Caplin ME, Davar J. Risk factors for the development and progression of carcinoid heart disease. Am J Cardiol. 2011 Apr 15;107(8):1221-6. doi: 10.1016/j.amjcard.2010.12.025. Epub 2011 Feb 4. PMID: 21296329.

15. Davar J, Connolly HM, Caplin ME, Pavel M, Zacks J, Bhattacharyya S, Cuthbertson DJ, Dobson R, Grozinsky-Glasberg S, Steeds RP, Dreyfus G, Pellikka PA, Toumpanakis C. Diagnosing and Managing Carcinoid Heart Disease in Patients With Neuroendocrine Tumors: An Expert Statement. J Am Coll Cardiol. 2017 Mar 14;69(10):1288-1304. doi: 10.1016/j.jacc.2016.12.030. PMID: 28279296.

16. Mota JM, Sousa LG, Riechelmann RP. Complications from carcinoid syndrome: review of the current evidence. Ecancermedicalscience. 2016 Aug 8;10:662. doi: 10.3332/ecancer.2016.662. PMID: 27594907; PMCID: PMC4990058.

17. Modlin IM, Pavel M, Kidd M, Gustafsson BI. Review article: somatostatin analogues in the treatment of gastroenteropancreatic neuroendocrine (carcinoid) tumours. Aliment Pharmacol Ther. 2010 Jan 15;31(2):169-88. doi: 10.1111/j.1365-2036.2009.04174.x. Epub 2009 Oct 21. PMID: 19845567.

18. Massimino K, Harrskog O, Pommier S, Pommier R. Octreotide LAR and bolus octreotide are insufficient for preventing intraoperative complications in carcinoid patients. J Surg Oncol. 2013 Jun;107(8):842-6. doi: 10.1002/jso.23323. Epub 2013 Apr 16. PMID: 23592524.

19. Guo LJ, Tang CW. Somatostatin analogues do not prevent carcinoid crisis. Asian Pac J Cancer Prev. 2014;15(16):6679-83. doi: 10.7314/apjcp.2014.15.16.6679. PMID: 25169508.

20. Condron ME, Pommier SJ, Pommier RF. Continuous infusion of octreotide combined with perioperative octreotide bolus does not prevent intraoperative carcinoid crisis. Surgery. 2016 Jan;159(1):358-65. doi: 10.1016/j.surg.2015.05.036. Epub 2015 Oct 23. PMID: 26603846.

21. Woltering EA, Wright AE, Stevens MA, Wang YZ, Boudreaux JP, Mamikunian G, Riopelle JM, Kaye AD. Development of effective prophylaxis against intraoperative carcinoid crisis. J Clin Anesth. 2016 Aug;32:189-93. doi: 10.1016/j.jclinane.2016.03.008. Epub 2016 Apr 20. PMID: 27290972.

22. Kinney MAO, Nagorney DM, Clark DF, O'Brien TD, Turner JD, Marienau ME, Schroeder DR, Martin DP. Partial hepatic resections for metastatic neuroendocrine tumors: perioperative outcomes. J Clin Anesth. 2018 Dec;51:93-96. doi: 10.1016/j.jclinane.2018.08.005. Epub 2018 Aug 8. PMID: 30098573.

23. Fouché M, Bouffard Y, Le Goff MC, Prothet J, Malavieille F, Sagnard P, Christin F, Hayi-Slayman D, Pasquer A, Poncet G, Walter T, Rimmelé T. Intraoperative carcinoid syndrome during small-bowel neuroendocrine tumour surgery. Endocr Connect. 2018 Dec;7(12):1245-1250. doi: 10.1530/EC-18-0324. PMID: 30352418; PMCID: PMC6240144.

24. Tapia Rico G, Li M, Pavlakis N, Cehic G, Price TJ. Prevention and management of carcinoid crises in patients with high-risk neuroendocrine tumours undergoing peptide receptor radionuclide therapy (PRRT): Literature review and case series from two Australian tertiary medical institutions. Cancer Treat Rev. 2018 May;66:1-6. doi: 10.1016/j.ctrv.2018.03.002. Epub 2018 Mar 16. PMID: 29602040.

25. Vaughan DJ, Brunner MD. Anesthesia for patients with carcinoid syndrome. Int Anesthesiol Clin. 1997 Fall;35(4):129-42. doi: 10.1097/00004311-199703540-00009. PMID: 9444534.

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DOI: https://dx.doi.org/10.17352/2455-2968.000149

26. Mancuso K, Kaye AD, Boudreaux JP, Fox CJ, Lang P, Kalarickal PL, Gomez S, Primeaux PJ. Carcinoid syndrome and perioperative anesthetic considerations. J Clin Anesth. 2011 Jun;23(4):329-41. doi: 10.1016/j.jclinane.2010.12.009. PMID: 21663822.

27. Powell B, Al Mukhtar A, Mills GH. Carcinoid: the disease and its implications for anaesthesia. Continuing Education in Anaesthesia Critical Care & Pain. 2011/02/01/;11(1):9-13.

28. Del Olmo-García MI, Muros MA, López-de-la-Torre M, Agudelo M, Bello P, Soriano JM, Merino-Torres JF. Prevention and Management of Hormonal Crisis during Theragnosis with LU-DOTA-TATE in Neuroendocrine Tumors. A Systematic Review and Approach Proposal. J Clin Med. 2020 Jul 12;9(7):2203. doi: 10.3390/jcm9072203. PMID: 32664679; PMCID: PMC7408760.

29. Lewis MA, Jaramillo S, Roberts L, Fleming CJ, Rubin J, Grothey A. Hepatic artery embolization for neuroendocrine tumors: postprocedural management and complications. Oncologist. 2012;17(5):725-31. PubMed PMID: 22511263. Pubmed Central PMCID: PMC3360912. Epub 2012/04/19.

30. Kinney MA, Warner ME, Nagorney DM, Rubin J, Schroeder DR, Maxson PM, Warner MA. Perianaesthetic risks and outcomes of abdominal surgery for metastatic carcinoid tumours. Br J Anaesth. 2001 Sep;87(3):447-52. doi: 10.1093/bja/87.3.447. PMID: 11517130.

31. Magabe PC, Bloom AL. Sudden death from carcinoid crisis during image-guided biopsy of a lung mass. J Vasc Interv Radiol. 2014 Mar;25(3):484-7. doi: 10.1016/j.jvir.2013.10.054. PMID: 24581473.

32. Fujie S, Zhou W, Fann P, Yen Y. Carcinoid crisis 24 hours after bland embolization: A case report. Biosci Trends. 2010 Jun;4(3):143-4. PMID: 20592464.

33. Del Prete M, Fiore F, Modica R, Marotta V, Marciello F, Ramundo V, Di Sarno A, Carratù A, di Roseto Cde L, Tafuto S, Tatangelo F, Baldelli R, Colao A, Faggiano A; Multidisciplinary Group for NeuroEndocrine Tumors of Naples. Hepatic arterial embolization in patients with neuroendocrine tumors. J Exp Clin Cancer Res. 2014 May 19;33(1):43. doi: 10.1186/1756-9966-33-43. PMID: 24887262; PMCID: PMC4038067.

34. Gupta S. Intra-arterial liver-directed therapies for neuroendocrine hepatic metastases. Semin Intervent Radiol. 2013 Mar;30(1):28-38. doi: 10.1055/s-0033-1333651. PMID: 24436515; PMCID: PMC3700796.

35. Granberg D, Garske U, Welin S, Kindmark H, Oberg K, Eriksson B, Nyman R. Selective internal radiation therapy in patients with carcinoid liver metastases. Acta Oncol. 2008;47(6):1169-71. doi: 10.1080/02841860701843738. PMID: 18607860.

36. De Keizer B, van Aken MO, Feelders RA, de Herder WW, Kam BL, van Essen M, et al. Hormonal crises following receptor radionuclide therapy with the radiolabeled somatostatin analogue [177Lu-DOTA0,Tyr3]octreotate. Eur J Nucl Med Mol Imaging. 2008 Apr;35(4):749-55. PubMed PMID: 18210106. Pubmed Central PMCID: PMC2668649. Epub 2008/01/23.

37. Morrisroe K, Sim IW, McLachlan K, Inder WJ. Carcinoid crisis induced by repeated abdominal examination. Intern Med J. 2012 Mar;42(3):342-4. doi: 10.1111/j.1445-5994.2012.02719.x. PMID: 22432991.

38. Kharrat HA, Taubin H. Carcinoid crisis induced by external manipulation of liver metastasis. J Clin Gastroenterol. 2003 Jan;36(1):87-8. doi: 10.1097/00004836-200301000-00031. PMID: 12488725.

39. Mehta AC, Rafanan AL, Bulkley R, Walsh M, DeBoer GE. Coronary spasm and cardiac arrest from carcinoid crisis during laser bronchoscopy. Chest. 1999 Feb;115(2):598-600. doi: 10.1378/chest.115.2.598. PMID: 10027471.

40. Janssen M, Salm EF, Breburda CS, van Woerkens LJ, de Herder WW, v/d Zwaan C, Roelandt JR. Carcinoid crisis during transesophageal echocardiography. Intensive Care Med. 2000 Feb;26(2):254. doi: 10.1007/s001340050060. PMID: 10784323.

41. Ozgen A, Demirkazik FB, Arat A, Arat AR. Carcinoid crisis provoked by mammographic compression of metastatic carcinoid tumour of the breast. Clin Radiol. 2001 Mar;56(3):250-1. doi: 10.1053/crad.1999.0167. PMID: 11247706.

42. Seymour N, Sawh SC. Mega-dose intravenous octreotide for the treatment of carcinoid crisis: a systematic review. Can J Anaesth. 2013 May;60(5):492-9. doi: 10.1007/s12630-012-9879-1. Epub 2013 Jan 18. PMID: 23328959.

43. Limbach KE, Condron ME, Bingham AE, Pommier SJ, Pommier RF. B-Adrenergic agonist administration is not associated with secondary carcinoid crisis in patients with carcinoid tumor. Am J Surg. 2019 May;217(5):932-936. doi: 10.1016/j.amjsurg.2018.12.070. Epub 2019 Jan 3. PMID: 30635207.

44. Condron ME, Jameson NE, Limbach KE, Bingham AE, Sera VA, Anderson RB, Schenning KJ, Yockelson S, Harukuni I, Kahl EA, Dewey E, Pommier SJ, Pommier RF. A prospective study of the pathophysiology of carcinoid crisis. Surgery. 2019 Jan;165(1):158-165. doi: 10.1016/j.surg.2018.04.093. Epub 2018 Nov 8. PMID: 30415870.

45. Welch TL, Pasternak JJ, Lanier WL. Anesthetic management of patients undergoing resection of carcinoid metastasis to the brain. J Clin Anesth. 2016 Aug;32:281-8. doi: 10.1016/j.jclinane.2015.08.014. Epub 2015 Sep 28. PMID: 26422777.

46. Howe JR, Cardona K, Fraker DL, Kebebew E, Untch BR, Wang YZ, Law CH, Liu EH, Kim MK, Menda Y, Morse BG, Bergsland EK, Strosberg JR, Nakakura EK, Pommier RF. The Surgical Management of Small Bowel Neuroendocrine Tumors: Consensus Guidelines of the North American Neuroendocrine Tumor Society. Pancreas. 2017 Jul;46(6):715-731. doi: 10.1097/MPA.0000000000000846. PMID: 28609357; PMCID: PMC5502737.

47. Ramage JK, Ahmed A, Ardill J, Bax N, Breen DJ, Caplin ME, Corrie P, Davar J, Davies AH, Lewington V, Meyer T, Newell-Price J, Poston G, Reed N, Rockall A, Steward W, Thakker RV, Toubanakis C, Valle J, Verbeke C, Grossman AB; UK and Ireland Neuroendocrine Tumour Society. Guidelines for the management of gastroenteropancreatic neuroendocrine (including carcinoid) tumours (NETs). Gut. 2012 Jan;61(1):6-32. doi: 10.1136/gutjnl-2011-300831. Epub 2011 Nov 3. PMID: 22052063; PMCID: PMC3280861.

48. National Heart LaBI. Study Quality Assessment Tools. U. S. Department Of Health & Human Services. [cited 2021]; Available from https://www.nhlbi.nih.gov/healthtopics/study-quality-assessment-tools.

49. Rinke A, Müller HH, Schade-Brittinger C, Klose KJ, Barth P, Wied M, Mayer C, Aminossadati B, Pape UF, Bläker M, Harder J, Arnold C, Gress T, Arnold R; PROMID Study Group. Placebo-controlled, double-blind, prospective, randomized study on the effect of octreotide LAR in the control of tumor growth in patients with metastatic neuroendocrine midgut tumors: a report from the PROMID Study Group. J Clin Oncol. 2009 Oct 1;27(28):4656-63. doi: 10.1200/JCO.2009.22.8510. Epub 2009 Aug 24. PMID: 19704057.

50. Radwan W, Lucke-Wold B, Robadi IA, Gyure K, Roberts T, Bhatia S. Neurosarcoidosis: unusual presentations and considerations for diagnosis and management. Postgrad Med J. 2017 Jul;93(1101):401-405. doi: 10.1136/postgradmedj-2016-134475. Epub 2016 Dec 5. PMID: 27920210; PMCID: PMC5500943.

51. Moor R, Goutnik M, Lucke-Wold B, Laurent D, Chen S, Friedman W, Rahman M, Allen N, Rivera-Zengotita M, Koch M. Clival Paraganglioma, Case Report and Literature Review. OBM Neurobiol. 2022;6(3):13. doi: 10.21926/obm.neurobiol.2203128. Epub 2022 Jul 7. PMID: 35844205; PMCID: PMC9280865.

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