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The Registry of Hyperthermic Intraperitoneal Chemotherapy – A Mandatory Step in the Development of this Therapeutic Approach in Romania

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Abstract
Multicenter/institutional studies have been the basis for the confirmation of Hyperthermic Intraperitoneal Chemotherapy as a therapeutic option for selected patients with Peritoneal Surface Malignancies. Starting from this model, using our experience in the implementation of a Diagnostic Laparoscopy for Abdominal Cancer database in surgical departments in Cluj-Napoca, we aimed to create a extended database, serving for Hyperthermic Intraperitoneal Chemotherapy. By coding the parameters of Hyperthermic Intraperitoneal Chemotherapy, which is a complex treatment both in terms of the equipment and techniques used and through the integration of different ways of approach (surgery, cytostatics drugs, hyperthermia), a Microsoft Access database was developed and implemented. The adoption and use of this database, followed by the implementation of a registry, will create the conditions required for the "coagulation" of individual experiences in Romania.

Keywords: Hyperthermic Intraperitoneal Chemotherapy; Peritoneal surface malignancies; Patient database; Treatment registries

Introduction

Hyperthermic Intraperitoneal Chemotherapy (HIPEC) preceded by Cytoreductive Surgery (CRS), represents a treatment standard for selected patients with Peritoneal Surface Malignancies (PSM) [1-4]. This approach has been confirmed by several multicenter studies (with the participation of hundreds of patients) [5-9] and by a few randomized clinical trials [10-12].

HIPEC treatment is concentrated in specialized centers in USA [3,13], Australia, Japan [14], France [5,9], Netherlands [11], Germany [15], Italy [8], Greece. The achievement of standards required by this therapeutic procedure is confirmed by the results obtained in reference centers, based on the ratio between risks (morbidity, mortality) and outcomes (survival, disease-free

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interval). In these centers, there are registries for HIPEC, which have allowed multicenter/institutional collaborations at national and international level.

The implementation of HIPEC treatment in Romania should be adapted to the existing particularities. There are initiatives regarding this therapeutic approach, but experience with it is just beginning. The treatment of PC by HIPEC is limited to the university centers in Constanţa [16], Târgu-Mureş, Braşov, Bucharest, and, more recently, Cluj-Napoca. The team led by Sârbu had the merit of introducing HIPEC in clinical practice in Romania [16], using the ANTIMETA device. Clinical experience with HIPEC is complemented by experimental and laboratory approaches [17-19].

Based on our previous experience with the implementation of a Diagnostic Laparoscopy for Abdominal Cancer database [20] - Diastal database [21], in all surgical clinics in Cluj-Napoca, we coded the particularities of HIPEC treatment and transferred them to a local database. The next step will be the implementation of a national registry, based on the data contained in local databases.

Particularities of HIPEC treatment

Equipment and technique of HIPEC

There are several types of devices for HIPEC [22, 23], but most of the equipment is based on the principle and the technical scheme proposed, as early as 1980, by Spratt [24]: heat exchanger, thermal sensors, pump, reservoir and tubing to ensure the cytostatic solution circuit. There are a number of international companies that produce HIPEC equipment (Table 1), all having high costs (around 100,000 euro).

Table 1. Equipment for HIPEC

HIPEC devices	Manufacturer/Representative
ThermoChem HT-2000	Therma Solutions (USA); www.thermasolutions.com
Performer HT	RanD SRL (Italy); info@rand-biotech.com
Cavitherm	Soramedical (France); www.cavitherm.com
SUNCHIP	GamidaTECH (France); www.gamidatech.com
EXIPER	Medica S.p.A. (Italy); www.menfis.it
Belmont HyperthermiaPump	Belmont Instruments (USA); www.belmontinstrument.com
VERATHERM	Thermal Therapeutic Systems (USA); www.thermaltherapeutics.com

Regarding the technical modality [25,26] for approaching HIPEC, there are two possibilities: after closing the abdomen (closed technique) or before closing the abdomen (open technique). The principal aim of the latter is to give the surgeon access to the peritoneal cavity. The major difference between the two techniques involves the increased risk of exposure to cytostatics for the staff in the operating room in the case of the open technique [27]. Several variants of the open technique, aimed at reducing this risk, have been described [28,29].

Specific CRS-HIPEC Training

The therapeutic approach of patients with PSM requires special training of the medical staff. The most important prognostic factors that are significantly correlated with the survival of patients treated by HIPEC are the "Peritoneal Cancer Index" (PCI) and the "Completeness of Cytoreduction" score [11,12]. These refer to the intraoperative staging of peritoneal tumor nodules (depending on the number of affected anatomical regions and on the size of nodules) and to the size of residual tumors after CRS. Both evaluations require the acquisition of the learning curve [30] by surgeons involved in CRS and HIPEC. The same is true about surgical techniques specific for PSM, generically termed "peritonectomies" [31]. A series of complementary procedures, such as hepatobiliary [32] and urinary procedures [33], have also been included in the arsenal of CRS.

The surgeon is not only responsible for surgery itself, but he must also have the skills required for conducting and supervising HIPEC, regardless of the technique used (closed or open). The efficiency of treatment depends on the maintenance of an intraperitoneal temperature between 41-43°C and on the "washing" of the entire peritoneal serosal surface with cytostatic solution [34]. In the case of the open technique (or its variants), the surgeon directly performs the thermal and spatial homogenization of the cytostatic solution in the peritoneal cavity, while in the closed technique, this mechanism is achieved by the control of the inflow and outflow of the cytostatic solution, by abdominal "assage" or by changing the position of the operating table [35,36].

The doctors of the anesthesia and intensive care team have to respond to multiple challenges. Thus, strict monitoring is required: invasive hemodynamic (Swan-Ganz catheterization, transesophageal Doppler echocardiographic monitoring); monitoring of respiratory flow, urinary flow, and of laboratory parameters (coagulation, thrombocytes, electrolytes, blood gases) [37,38].

HIPEC Variables

A number of variables have been described, which condition the obtaining of the expected results of HIPEC: intraperitoneal temperature; the intraperitoneally administered dose of cytostatic drugs; the type and volume of the cytostatic solution, the duration of contact between the cytostatic and the peritoneum, the use of vasoactive agents, and macromolecules [34]. Temperature is monitored in the peritoneal cavity in a variable number of sites, as well as at the entrance/exit of the cytostatic solution to and from the peritoneal cavity. Core body temperature is monitored at esophageal or at urinary bladder level. The time allocated to HIPEC varies between 30-90 minutes, depending on the cytostatic used.

The Multidisciplinary Team in the PSM Treatment

The treatment of patients with PSM by HIPEC has not been free of controversies. The point of view of oncologists, followers of systemic chemotherapy, considered that for HIPEC, risks exceeded benefits [3]. In reality, HIPEC and systemic chemotherapy are not competitive treatments, the best results are obtained by integrating the two modalities [39], so that therapeutic decision for patients with PSM should be made by multidisciplinary teams.

Registry of HIPEC Treatment

Coding of HIPEC parameters

In centers specialized in HIPEC, there are different approaches to this treatment, which involve all the mentioned aspects (equipment, technique, clinical parameters, variables, integration of systemic chemotherapy). Moreover, new research directions have emerged which are aimed at developing laparoscopic HIPEC [40,41], as a method for the prophylaxis of secondary PMS [42] and as an iterative method for the treatment of PMS recurrences [43].

Only for colorectal cancer, consensus regarding the clinical parameters of HIPEC treatment [44] and HIPEC variables [45] has been reached. Thus, if certain parameters can be coded in order to be included in database (Table 2), for others, "text" variables were used.

Table 2. Coding of HIPEC parameters for inclusion in database

HIPEC treatment	Coding
Previous surgery	pop-down lists (absent; optimal; suboptimal)
Previous systemic chemotherapy	pop-down lists (absent; optimal; suboptimal)
Perioperative neoadjuvant systemic chemotherapy	"yes/no" value
Bidirectional systemic chemotherapy	
Postoperative intraperitoneal chemotherapy	
HIPEC treatment	pop-down lists (radical; prophylactic; iterative)

Karnofschy Performance Index (%)	"number" value (0-100)
Weight (kg)	"number" value
Height (cm)	
Ascites (ml)	
Peritonectomies	parietal; pelvic; omental bursa; right diaphragmatic; left diaphragmatic: "yes/no" value
Particular topographies	liver capsule; mesentery; small intestinal serosa; stomach serosa; falciform ligament; subpyloric space; hepatic pedicle: "yes/no" value
Visceral resections	greater omentum; lesser omentum; rectosigmoid; ovaries; uterus; right hemicolon; left hemicolon; gallbladder; spleen; pancreas; stomach; liver; bile ducts; urinary bladder; ureter; other: "yes/no" value
Anastomoses	colo-rectal; colo-colic; entero-colic; entero-rectal; entero-enteral; gastro-enteric: "yes/no" value
Ostomies	colostomy; enterostomy: "yes/no" value
Equipment	"text" value
Technique	pop-down lists (closed; open; open variants)
Peridural catheter	"yes/no" value
Swan-Ganz catheter	
Transesophageal Doppler echocardiography	
Intraperitoneal thermal sensors	"number" value
Core temperature	urinary bladder; endoesophageal: "yes/no" value
Intraperitoneal pressure sensor	"yes/no" value
Pleural drainage	
Cytostatic drug 1, dose prescribed (mg)	"text" value
Cytostatic drug 1, dose prescribed (mg)	
Circulating solution type, volume (ml)	
Vasoactive agents	"yes/no" value
Macromolecular agents	
Homogenization (for the closed technique)	abdominal massage; change of the operating table position; flow variation: "yes/no" value
Peritoneal Cancer Index	"number" value (0-39); calculation function implementation
"Completeness of Cytoreduction" score	pop-down lists (0; 1; 2; 3)
Start/end of surgery	"data" value
Start/end of HIPEC	

The Peritoneal Cancer Index (PCI), established at the time of surgery, according to a protocol developed by Sugarbaker [45], is a synthesis of both the distribution (in 13 predefined abdominopelvic regions) and the size of peritoneal metastases (based on the lesion score).

At the level of the abdominal wall, 9 regions (0-8) are delimited, by establishing two transverse planes and two sagittal planes. The upper transverse plane is located at the lower border of the costal margin, and the lower transverse plane is at the level of the anterior superior iliac spine. The sagittal planes divide the abdomen into three equal sectors. Thus, nine compartments are evidenced, which are numbered clockwise: 0 – center of abdomen, 1 – right upper region (right hypochondrium), 2 - epigastrium, 3 – left upper region (left hypochondrium), 4 – left flank, 5 – left lower region (left iliac fossa), 6 - pelvis, 7 – right lower region (right iliac fossa), 8 – right flank. The regions from 9 to 12 divide the small intestine into upper jejunum and lower jejunum, and upper ileum and lower ileum, respectively.

From each region, lesion score (LS) represents the largest diameter of peritoneal nodules: LS 0 – no malignant deposits are visualized; LS 1 – tumor nodules smaller than 0.5 cm; LS 2 – nodules between 0.5 and 5 cm; LS 3 – tumor nodules larger than 5 cm or confluence of tumor nodules. The primary tumor and the local recurrences that can be completely removed are excluded from the evaluation. LS are calculated for each of the 13 abdomino-pelvic regions, and the sum of the LS is PCI, whose values may range between 0 and 39 (Table 3).

Table 3. Coding and implementation of PCI

Regions	Coding	Lesion Score
Region *i*, $i \in \{1,2,3,\ldots,13\}$	"number" value (0,1,2,3)	v_i, $i \in \{1,2,3,\ldots,13\}$
PCI	"number" value (0-39)	$\sum_1^{13}(v_i)$

PCI = Peritoneal Cancer Index

HIPEC Database

In the first stage, the HIPEC database ("DB-HIPEC Treatment") was developed using the Microsoft Access 2000 engine, the reason being that its flexible structure makes the database easy to adapt to the requirements of each particular doctor. This is the reason for the choice of this software. In addition, the great majority of doctors are currently acquainted with the Microsoft Office package, so that it's use should not pose particular problems.

The fields/lines of the database (HIPEC parameters) were defined based on the coding in Table 2. "True/false" fields were mainly used, and "pop-down lists" were predefined. As HIPEC is implemented and standardized, "text" or "number" fields will be replaced by predefined fields.

This is a multi-table database with a hierarchically subordinate structure: "DB-HIPEC Treatment" is included in the database of patients with PSM ("DB-PSM"), which in turn is included in a database of patients with malignancies ("DB-patient"). The relationships between the main table, containing the patient's identification data, and the other tables were defined in the majority of the situations as "One-To-Many", given the fact that the contained parameters are dynamically monitored. "One-To-One" relationships were also defined for tables containing information about "family doctors", "location", and "staging", with the mention that these can in turn undergo changes in dynamics (the relationships will have to be redefined as "One-To-Many", Figure 1).

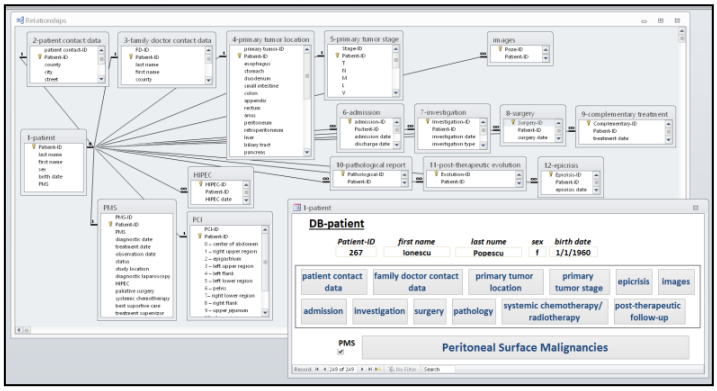


Figure 1. Multi-table structure and relationships in the "DB-patient"; "DB-patient" design

The design is based on a view of the main "DB-patient", from which specific details found in the relational databases: in a first stage, "DB-PSM" (Figure 2) and subsequently, "DB-HIPEC Treatment" (Figure 3), can be reached through buttons (the names suggest the destination).

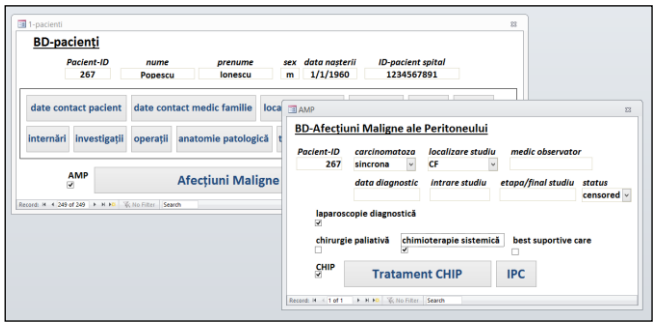


Figure 2. "DB-PSM" design, integrated in "DB-patient"

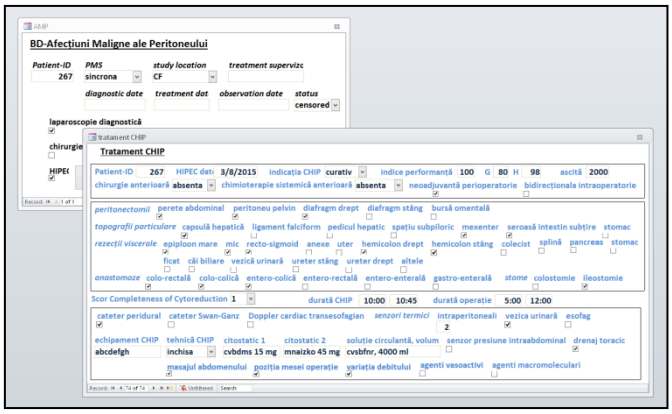


Figure 3. "DB-HIPEC Treatment" design, integrated in "DB-PSM"

The calculation of PCI required the implementation of a function, according to Table 3. This required the creation of a PCI database ("DB-PCI") included in "DB-HIPEC Treatment", for which a "One-To-One" relationship was defined (for each HIPEC treatment, a single PCI is calculated, Figure 4).

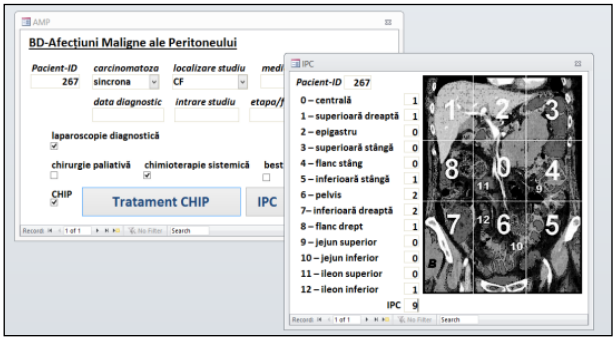


Figure 4. "DB-PCI" design, integrated in "DB-PSM"

At the local level of the database in the clinic, the security groups are those classical for relational databases: administrator and authorized user.

HIPEC Registry

In a second stage, for the management and processing of data coming from different centers, the team will develop, in SqlServer, a global registry, situated in cloud. This registry benefits from the many advantages offered by this technology: performance, safety, scalability, accessibility. Being a registry, it does not contain all information collected by doctors in the local databases (Table 4). This is also a necessary condition for security reasons. The patients' identification data will not be entered in the registry. In contrast, each entry in the registry will have a unique identifier, based on which, with the required authority, the patient's record can be identified at local level, for detailed consultation.

Synchronization between the local databases and the global registry will be performed by automatic procedures, which will run at determined time intervals, avoiding in this way the overloading of the system.

For the global registry, there are two categories of users: specific procedure users, which will be used in the case of automatic synchronization procedures, between local databases and the registry; and users corresponding to the persons involved in the use of the registry. If in the first case, procedure users will have the right to perform only predefined command sequences, person users

will have access rights corresponding to the function of each.

Table 4. Coding of HIPEC treatment, for inclusion in the registry

Patient-ID	"Autonumber" value; related to local database patient
Name of treatment supervisor	"text" value
Phone number of treatment supervisor	"number" value
Mail adress of treatment supervisor	"text" value
Hospital of treatment supervisor	"text" value
Locality of treatment	pop-down lists (Cluj-Napoca; Braşov; Târgu-Mureş; Bucureşti; Constanţa; altele)
Date of HIPEC treatment	"data" value
Primary tumour	pop-down lists (peritoneum; colon; appendix; ovary; rectum; stomach; pseudomyxoma peritonei; other)
Equipment	"text" value
HIPEC treatment	pop-down lists (first; iterative)
HIPEC approach	pop-down lists (open; laparoscopic)
Cytoreductive surgery	"yes/no" value
Previous surgery	pop-down lists (absent; optimal; suboptimal)
Previous systemic chemotherapy	pop-down lists (absent; optimal; suboptimal)
Perioperative systemic chemotherapy	"yes/no" value

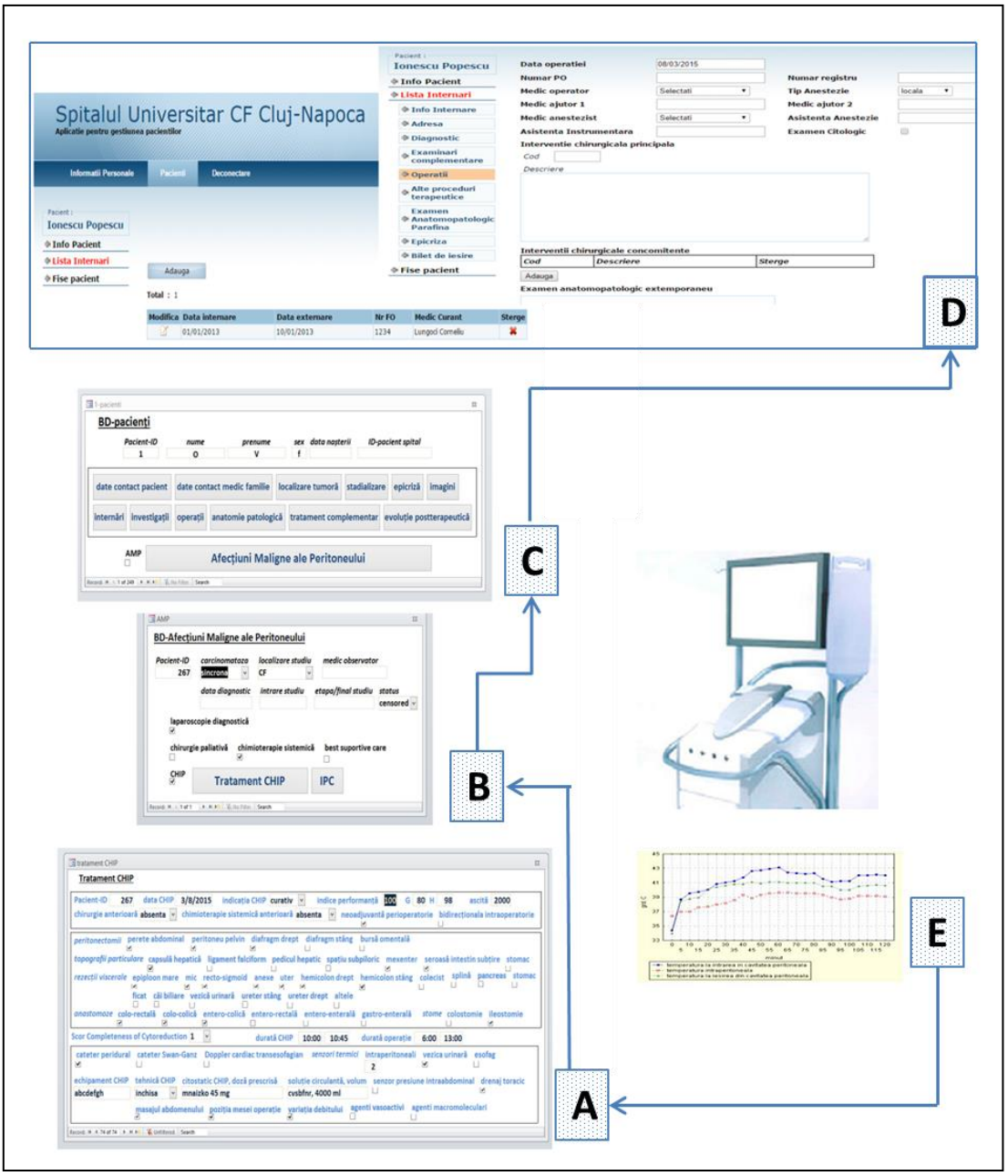
Results and Discussions

In Romania, the approach of PMS by HIPEC is available, but the access of patients to treatment is extremely limited. In Germany, the treatment and monitoring of patients with PMS are performed with the financial implication of the Health Insurance Authority, according to therapeutic guidelines, within national registries [15]. Non-governmental organizations also participate in the financial support of CRS-HIPEC treatment [46].

Due to the specific pathology, the access to the information contained in the registry will be very well controlled. Access to the registry will be automatic (through synchronization procedures) or by authentication. A policy to stipulate the exact conditions under which information can be made available to accredited users and what information can be made available, as well as the steps to follow and the documentation to complete for each procedure will be required.

The "DB-HIPEC Treatment" model (treatment module) will be used to code and develop the other specific modules within "DB-PSM": "clinical examination", "investigations", "posttherapeutic evolution".

The development of "DB-HIPEC Treatment" and "DB-PSM" can be achieved by three directions: pathway (1) - by integration in "DB-patient" (data base of patients with malignancies), after its development (Figure 5: A⇒B⇒C); pathway (2) - by integration in the hospital database (Figure 5: A⇒B⇒C⇒D); pathway (3) - by import of data, like intraperitoneal temperature, solution flow, from the equipment used (Figure 5: C⇒A). The most accessible of these is pathway (1), the other two being dependent on the collaboration with proprietary licensed software companies.



"**Figure 5.** Opportunities for the development of "DB-PSM" and "DB-HIPEC Treatment" (A="DB-HIPEC Treatment"; B="DB-PSM"; C="DB-patient"; D=hospital database; E= HIPEC equipment)

Although the chosen technology allows access to databases using mobile equipment, the purpose of developing this registry (to provide a specific data source for those who are interested in this problem and authorized to obtain these data) makes the probability of access by using such equipment relatively low. In addition, the emerging stage of implementation of data access standards between different mobile technology manufacturers makes the implementation of these functions difficult.

Similarly to the registry development for the HIPEC treatment of PSM, applications can be developed for Liver Metastases or locally advanced Abdominal Cancers

Conclusion

The database of HIPEC must be adopted, used, and verified in Romanian centers involved in the administration of this treatment, in order to facilitate collaborations with a common starting point. Thus, significant data will be collected, which will allow assessing therapeutic results and standardizing HIPEC. These will also the base for the implementation of national/regional registries, which, under the conditions of dedicated health care management of HIPEC, will allow the approach of patients with PSM to move to a higher level in Romania.

List of abbreviations

HIPEC - Hyperthermic Intraperitoneal Chemotherapy;
CRS - Cytoreductive Surgery;
PSM - Peritoneal Surface Malignancies;
PCI - Peritoneal Cancer Index;
LS - lesion score;
"DB-HIPEC" - Hyperthermic Intraperitoneal Chemotherapy database;
"DB-PSM" - Peritoneal Surface Malignancies patients database;
"DB-patient"-Cancer patients database;
"DB-PCI"- Peritoneal Cancer Index patients database

Conflict of Interest

The authors declare that they have no conflict of interest.

Authors' Contributions

CL, IAM carried defined the aim and the design of research. CL, TC carried out the experiments. VM participated in the design of the study and performed the interpretation of data. CL, OO, RB coordinates and helped to draft the manuscript. All authors read and approved the final manuscript.

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References

1. Randle RW1, Swett KR, Swords DS, Shen P, Stewart JH, Levine EA, Votanopoulos KI. Efficacy of Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy in the Management of Malignant Ascites. Ann Surg Oncol 2014;21(5):1474-1479.
2. Kuijpers A, Aalbers A, Nienhuijs S, de Hingh I, Wiezer M, van Ramshorst B, et al. Implementation of a Standardized HIPEC Protocol Improves Outcome for Peritoneal Malignancy. World J Surg 2015;39(2):453-460.
3. Sugarbaker PH, Ryan DP. Cytoreductive surgery plus hyperthermic perioperative chemotherapy for selected patients with peritoneal metastases from colorectal cancer: a new standard of care or an experimental approach? Gastroenterol Res Pract [Internet]. 2012 Jan [cited 2013 Aug 3];2012:309417. Available from:

http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3408708&tool=pmcentrez&rendertype=abstract
4. Levine E, Stewart J, Shen P, Russell G, Loggie B, Votanopoulos K. Intraperitoneal chemotherapy for peritoneal surface malignancy: experience with 1,000 patients. J Am Coll Surg. 2014;218(4):573-585.
5. Elias D, Gilly F, Boutitie F, Quenet F, Bereder J-M, Mansvelt B, et al. Peritoneal colorectal carcinomatosis treated with surgery and perioperative intraperitoneal chemotherapy: retrospective analysis of 523 patients from a multicentric French study. J Clin Oncol 2010;28(1):63-68.
6. Bakrin N, Bereder J, Decullier E, Classe J, Msika S, Lorimier G, et al. Peritoneal carcinomatosis treated with cytoreductive surgery and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for advanced ovarian carcinoma: a French multicentre retrospective cohort study of 566 patients. Eur J Surg Oncol 2013;1435-1443.
7. Kobayashi H, Kotake K, Sugihara K. Outcomes of surgery without HIPEC for synchronous peritoneal metastasis from colorectal cancer: data from a multi-center registry. Int J Clin Oncol 2014;19(1):98-105.
8. Cavaliere F, De Simone M, Virzì S, Deraco M, Rossi CR, Garofalo A, et al. Prognostic factors and oncologic outcome in 146 patients with colorectal peritoneal carcinomatosis treated with cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy: Italian multicenter study S.I.T.I.L.O. Eur J Surg Oncol 2011;37(2):148-154.
9. Elias D, Gilly F, Quenet F, Bereder JM, Sidéris L, Mansvelt B, et al. Pseudomyxoma peritonei: a French multicentric study of 301 patients treated with cytoreductive surgery and intraperitoneal chemotherapy. Eur J Surg Oncol 2010;36(5):456-462.
10. Yang X-J, Huang C-Q, Suo T, Mei L-J, Yang G-L, Cheng F-L, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy improves survival of patients with peritoneal carcinomatosis from gastric cancer: final results of a phase III randomized clinical trial. Ann Surg Oncol 2011;18(6):1575-1581.
11. Verwaal VJ, van Ruth S, de Bree E, van Sloothen GW, van Tinteren H, Boot H, et al. Randomized trial of cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy and palliative surgery in patients with peritoneal carcinomatosis of colorectal cancer. J Clin Oncol 2003;21(20):3737-3743.
12. Rudloff U, Langan R, Mullniax J, Beane J, Steinberg S, Beresnev T, et al. Impact of maximal cytoreductive surgery plus regional heated intraperitoneal chemotherapy (HIPEC) on outcome of patients with peritoneal carcinomatosis of gastric origin: results of the GYMSSA trial. J Surg Oncol 2014;110(3):275-284.
13. Esquivel J, Sticca R, Sugarbaker P, Levine E, Yan TD, Alexander R, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in the management of peritoneal surface malignancies of colonic origin: a consensus statement. Society of Surgical Oncology. Ann Surg Oncol 2007;14(1):128-133.
14. Fujimura T, Yonemura Y, Fushida S. Continuous hyperthermic peritoneal perfusion for the treatment of peritoneal dissemination in gastric cancers and subsequent second-look operation. Cancer 1990;65(1):65-71.
15. Piso P, Leebmann H, März L, Mayr M. Cytoreductive surgery for malignant peritoneal tumors. Chirurg 2015;86(1):38-46.
16. Sârbu V, Maciuceanu B, Supeanu I, Dima S, Parvu M, Davidescu C, et al. Preliminary data about Intraperitoneal Chemohyperthermia in abdominal organs cancers. Chirurgia (Bucur) 2007;102(5):549-555.
17. Lungoci C, Raus I, Oniu T, Moga D, Stroia N, Muntean V, et al. Assessment of temperature distribution in intraperitoneal chemohyperthermia. In: Ciupa RV, Vlad S, editors. IFMBE Proceeding. Cluj-Napoca; 2014, p. 193-196.
18. Lungoci C, Septimiu T, Galasiu R. Device proposed for Intraperitoneal Chemohyperthermia. Acta Medica Transilv 2004;1(4):86-68.
19. Lungoci C, Septimiu T, Galasiu R. Device for Intrapritoneal Chemohyperthermia-experimental studies. Acta Medica Transilv 2004;1(4):85-88.

20. Muntean V, Oniu T, Lungoci C, Fabian O, Munteanu D, Molnar G, et al. Staging laparoscopy in digestive cancers. J Gastrointest Liver Dis 2009;18(4):461-467.
21. Călinici T, Muntean V, Bacârea V. DIASTAL – a client server database application for Laparoscopic Diagnosis and Staging in Abdominal Cancers. Appl Med Inform 2005;17(3):68-71.
22. Ortega-Deballon P, Facy O, Magnin G, Piard F, Chauffert B, Rat P. Using a heating cable within the abdomen to make hyperthermic intraperitoneal chemotherapy easier: feasibility and safety study in a pig model. Eur J Surg Oncol 2010;36(3):324-328.
23. Cho CH, Wust P, Hildebrandt B, Issels RD, Sehouli J, Kerner T, et al. Regional hyperthermia of the abdomen in conjunction with chemotherapy for peritoneal carcinomatosis: evaluation of two annular-phased-array applicators. Int J Hyperthermia 2008;24(5):399-408.
24. Spratt JS, Adcock RA, Muskovin M, Sherrill W, Mckeown J. Clinical Delivery System for Intraperitoneal Hyperthermic Chemotherapy. Cancer Res 1980;40:256-260.
25. Sugarbaker PH. Technical Handbook for the Integration of Cytoreductive Surgery and Perioperative Intraperitoneal Chemotherapy into the Surgical Management of Gastrointestinal and Gynecologic Malignancy 4 th Edition Technical Handbook for the Integration of Cytoreductive. 4th Editio. The Ludann Company Grand Rapids, Michigan; 2005.
26. Elias D, Antoun S, Goharin A, Otmany A, Puizillout J, Lasser P. Research on the best chemohyperthermia technique of treatment of peritoneal carcinomatosis after complete resection. Int J Surg Investig 2000;1(5):431-439.
27. González-Moreno S, González-Bayón L, Ortega-Pérez G. Hyperthermic intraperitoneal chemotherapy: methodology and safety considerations. Surg Oncol Clin N Am 2012;21(4):543-557.
28. Ortega-Deballon P, Facy O, Jambet S, Magnin G, Cotte E, Beltramo J, et al. Which Method to Deliver Hyperthermic Intraperitoneal Chemotherapy with Oxaliplatin? An Experimental Comparison of Open and Closed Techniques. Ann Surg Oncol 2010;17(7):1957-1963.
29. Fujimura T, Yonemura Y, Fushida S. Continuous hyperthermic peritoneal perfusion for the treatment of peritoneal dissemination in gastric cancers and subsequent second-look operation. Cancer 1990;65(1):65-71.
30. Kusamura S, Baratti D, Virzì S, Bonomi S, Iusco D, Grassi A, et al. Learning curve for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in peritoneal surface malignancies: analysis of two centres. J Surg Oncol 2013;107(4):312-319.
31. Sugarbaker P. Peritonectomy Procedures. Ann Surg 1995;221(1):29-42.
32. Glockzin G, Renner P, Popp FC, Dahlke MH, von Breitenbuch P, Schlitt HJ, et al. Hepatobiliary procedures in patients undergoing cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. Ann Surg Oncol 2011;18(4):1052-1059.
33. Leapman M, Jibra G, Tabrizian P, Franssen B, Yang M, Romanoff A, et al. Genitourinary resection at the time of cytoreductive surgery and heated intraperitoneal chemotherapy for peritoneal carcinomatosis is not associated with increased morbidity or worsened oncologic outcomes: a case-matched study. Ann Surg Oncol 2014;21(4):1153-1158.
34. Sugarbaker PH, Speeten K Van Der, Stuart OA, Cancer W. Pharmacologic rationale for treatments of peritoneal surface malignancy from colorectal cancer. World J Gastrointest Oncol 2010;2(1):19-30.
35. Sugarbaker P. An instrument to provide containment of intraoperative intraperitoneal chemotherapy with optimized distribution. J Surg Oncol 2005;92:142-146.
36. Chua TC, Pelz JOW, Morris DL. Surgery for colorectal peritoneal carcinomatosis. Scand J Gastroenterol 2012;47(3):277-285.
37. Esquivel J, Angulo F, Bland RK, Stephens a D, Sugarbaker PH. Hemodynamic and cardiac function parameters during heated intraoperative intraperitoneal chemotherapy using the open "coliseum technique". Ann Surg Oncol 2000;7(4):296-300.
38. Webb CA-J, Weyker PD, Moitra VK, Raker RK. An overview of cytoreductive surgery and hyperthermic intraperitoneal chemoperfusion for the anesthesiologist. Anesth Analg. 2013;116(4):924-931.

39. Franko J, Ibrahim Z, Gusani NJ, Holtzman MP, Bartlett DL. Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemoperfusion Versus Systemic Chemotherapy Alone for Colorectal Peritoneal Carcinomatosis. Cancer 2010;116:3756-3762.
40. Valle M, Van der Speeten K, Garofalo A. Laparoscopic hyperthermic intraperitoneal peroperative chemotherapy (HIPEC) in the management of refractory malignant ascites: A multi-institutional retrospective analysis in 52 patients. J Surg Oncol 2009;100(4):331-334.
41. Ba M-C. Chemotherapy with laparoscope-assisted continuous circulatory hyperthermic intraperitoneal perfusion for malignant ascites. World J Gastroenterol 2010;16(15):1901-1905.
42. Sammartino P, Sibio S, Biacchi D, Cardi M, Accarpio F, Mingazzini P, et al. Prevention of Peritoneal Metastases from Colon Cancer in High-Risk Patients: Preliminary Results of Surgery plus Prophylactic HIPEC. Gastroenterol Res Pract [Internet]. 2012 Jan [cited 2012 Aug 13];2012:141585. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3356888&tool=pmcentrez&rendertype=abstract
43. Votanopoulos KI, Ihemelandu C, Shen P, Stewart JH, Russell GB, Levine E. Outcomes of Repeat Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy for the Treatment of Peritoneal Surface Malignancy. J Am Coll Surg 2012;215(3):412-417.
44. Turaga K, Levine E, Barone R, Sticca R, Petrelli N, Lambert L, et al. Consensus Guidelines from The American Society of Peritoneal Surface Malignancies on Standardizing the Delivery of Hyperthermic Intraperitoneal Chemotherapy (HIPEC) in Colorectal Cancer Patients in the United States. Ann Surg Oncol 2014;21(5):1501-1505.
45. Jacquet P, Sugarbaker PH. Clinical research methodologies in diagnosis and staging of patients with peritoneal carcinomatosis. Cancer Treat Res 1996;82:359-374.
46. Konigsrainer A. A new therapy concept for peritoneal carcinomatosis. © BIOPRO Baden-Württemberg GmbH [Internet] 2008 [cited 2014 September 10]. Available from: http://www.bio-pro.de/magazin/wissenschaft/archiv_2008/index.html?lang=en&artikelid=/artikel/01543/index.html