ORIGINAL ARTICLE / Gastrointestinal imaging

Medico-economic study of the management of hepatocellular carcinoma by chemo-embolization


Abstract

Purpose: This study has two aims. The first is to compare conventional lipiodol chemo-embolization (Trans Arterial Chemo-Embolization — TACE) to one using pre-loaded particles (Trans Arterial Chemo-Embolisation-Drug Eluted Bead — TACE-DEB) using a cost minimization study. The second is to define the fundable nature of TACE-DEB and the conditions under which it is cost-effective.

Materials and methods: Retrospective study of patients treated by chemo-embolization (n = 31: TACE; n = 32: TACE-DEB) during the year 2010. The cost minimization study was conducted from the hospital perspective. Direct medical costs were calculated and compared using the readjusted ENCC (National Studies of Costs by Common Methodology) method. The affordability of the two techniques and definition of a cost-effective hypothesis (break-even point) were also established.

Results: All DRGs combined, lengths of stay (TACE: 4.90 ± 3.36; TACE-DEB: 5.03 ± 3.36) does not change significantly. An average upper mean cost for TACE-DEB is described (TACE: 2869.05 €; TACE-DEB: 3960.10 €). The affordability calculations in the study show that, overall, TACE-DEB can be funded regardless of DRG. A ratio of 1.3 procedures using the conventional (TACE) method would enable TACE-DEB procedures to be funded.

Conclusion: This medico-economic analysis demonstrates that the TACE-DEB procedure is fundable.

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* Corresponding author.
E-mail address: johann.clouet@chu-nantes.fr (J. Clouet).
Liver cancer, or hepatocellular carcinoma (HCC), is the third leading cause of cancer deaths throughout the world [1]. It is the fifth most common cancer in the world and has an estimated incidence of approximately 700,000 new cases annually [2]. Because it is paucisymptomatic resulting in late diagnosis, only a third of patients suffering from HCC are eligible for curative treatment. Clinicians offer palliative care with embolization of the feeder vessels for two-thirds of inoperable, non-metastatic HCC (Child A-B, intermediary stage by the BCLC [Barcelona Clinic Liver Cancer] classification [1,2]). Two embolization approaches are currently available using interventional radiology techniques. The first is based on the principle of injecting a chemotherapy emulsified in lipiodol followed by vascular embolization with resorbable particles. This is the conventional technique or TACE (Trans Arterial Chemo-Embolization). The second more recent technique uses non-resorbable microspheres loaded with cytotoxic agents, usually doxorubicin. These are carried out in a single interventional stage and are commonly called TACE-DEB (TACE-Drug Eluting Beads).

Both techniques have been shown to offer similar efficacy in terms of patient’s length of survival [3]. TACE-DEB has significant technical advances as it does not require extemporary preparation; light anesthesia can be given and liver function is protected by targeted chemo-embolization. Access to this latest technique in healthcare establishments is currently still limited, particularly because of a lack of specific reimbursement by the health insurance system. The economic and organizational landscape of the healthcare system in France changed greatly in 2004 with the hospital funding reforms and introduction of activity based tariffs (TAA) (law no. 2003-1199 of 18 December 2003). As such, healthcare establishments are funded by their activity (type and volume of procedures) by amounts linked to the hospital stays (SRG: Stay Reference Group). In parallel, and in order to allow access to expensive new medicinal products and devices (MD), a list of reimbursable products in addition to the SRG was introduced. This system is limited in terms of the time delay to approve new procedures and devices, particularly new technological and therapeutic developments such as the TACE-DEB technique. The cost of this new technique is therefore only partially covered by the stay tariff.

As TACE-DEB and TACE are similarly effective, and in view of the technical advantages of TACE-DEB and its lack of reimbursement we set out to conduct a medico-economic study to support healthcare establishments in making decisions.

We have carried out a retrospective medico-economic cost minimization analysis to establish the least expensive chemo-embolization technique from the hospital’s perspective [4]. The cost minimization analysis is the main aim of this study. In parallel, a secondary objective was to establish whether or not chemo-embolization was fundable for the establishment, based on a affordability analysis and measurement of the break-even point.

Materials and methods

Patients

This retrospective study was carried out on patients suffering from inoperable, non-metastatic HCC. The patients received a course of hepatic chemo-embolization between 1st January 2010 and 31st December 2010 at the Nantes University Hospitals, either TACE (26 patients) or TACE-DEB (24 patients). Each course received by the patient was deemed to be a new procedure. No age or sex criteria were included. The different stages of the liver disease were defined according to the Barcelona classification. Post-hospital admission consequences were not included. The doxorubicin-loaded particles used were DC-Beads™ (Terumo, Louvain, Belgium) and the (lipiodol) embolization particles used for the TACE were either resorbable (Gelatins: Gelitason or Geliputty™, Gelita Medical, Estissac, France) or non-resorbable (Embogold™ calibrated particles, Merit Medical, Voisins le Bretonneux, France).

Treatments

The indication for TACE or TACE-DEB was decided in a weekly multidisciplinary meeting attended by a radiologist, a surgeon, a gastroenterologist, an oncologist and a radiotherapist. The decisions were consistent with the guidelines from the Barcelona conference [5] and the TACE and TACE-DEB procedures were carried out using standard protocols in the Departments of Radiology. In both treatment types, the angiographic techniques used involved catheterization of the hepatic artery from a femoral approach and then selective catheterization of the arterial pedicles feeding the tumors. In the case of TACE, this was followed by infusion of an emulsion containing 10 mL of Lipiodol™ (Guerbet, France) and doxorubicin (50–75 mg/m²) followed by embolization with hemostatic gelatin fragments or microspheres, depending on angiographic findings and the operator’s usual practice until flow stagnated in the 2nd and 3rd order branches of the hepatic artery. In the case of TACE-DEB, treatment involved an injection of a mixture of 4 mL of DC-Bead™ loaded with 150 mg of doxorubicin and non-ionic iodinated contrast medium.

Cost minimization study

Perspective

The perspective used was that of the hospital, counting expenditure related to the length of stay for each procedure and DRG (Diagnostic Reference Group) costs according to the ENCC (French National Scale for Common Methodology Costs) [6], readjusted for the actual length of stay in the establishment.

Measurement of costs

As the cost minimization study was retrospective, we considered the direct medical costs which were analyzed using the readjusted ENCC method [6]. Briefly, DRGs are used to estimate the costs from PMSI data (Programme to Medicalise Information Systems) and from ENCC. Average national costs are reprocessed in order to apply to the establishment in which the study is being carried out. Allocation to different expenditure lines is used to obtain two types of costs: fixed and variable. The fixed costs are clinical expenditure, logistics, and general administration and are applied on a daily basis to obtain a fixed daily cost. Variable costs do not
depend on length of stay and are the medical and technical expenditure and costs directly related to the patient [7].

The DRG categories examined in this study were “malignant hepatobiliary or pancreatic system disorders” from level 1 (no significant severity) to level 4 (major severity) representing the severity levels from each of the patients. These severity levels take account of case severity by incorporating associated complications or morbidities. Each DRG has a tariff, which is shown in Table 1.

Calculation of consumable costs
All of the IMD and other consumables required for the procedure were recorded and their costs were calculated from the hospitals’ agreed tender prices. A microcosting analysis was carried out to prepare the loaded particles in the UPCO (Clinical and Oncology Pharmacy Unit). This method was used to precisely establish the resources used by each patient in a procedure: surgical time, equipment used, laboratory investigations and imaging, etc. Calculation of resources the resources consumed was used to establish the actual costs attributable to the different strategies (Table 2).

Calculation of establishment hospitalization costs
The DRG representing the different stays chosen were provided by the Nantes University Hospital Medical Information Department (DIM). The related lengths of stay were recovered from the Nantes University Hospitals with Clinicom™ software (Intersystems France, Paris, France). The fixed and variable costs were weighted by DRG and length of stay.

SRG reimbursement
The Nantes University Hospital DIM searched for the theoretical and actual SRG reimbursement rates for each procedure carried out during the study period.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>List of DRG linked to the SRG 2010 tariffs and upper and lower limits.</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRG</td>
<td>Wording</td>
</tr>
<tr>
<td>07M061</td>
<td>Malignant, hepatobiliary or pancreatic system disorders, level 1</td>
</tr>
<tr>
<td>07M062</td>
<td>Malignant, hepatobiliary or pancreatic system disorders, level 2</td>
</tr>
<tr>
<td>07M063</td>
<td>Malignant, hepatobiliary or pancreatic system disorders, level 3</td>
</tr>
<tr>
<td>07M064</td>
<td>Malignant, hepatobiliary or pancreatic system disorders, level 4</td>
</tr>
</tbody>
</table>

*Lower exemption limit; **upper exemption limit.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Description of medical devices used depending on the type of embolization.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of embolization</td>
<td>TACE conv.</td>
</tr>
<tr>
<td>Embolization agents or IMD</td>
<td>1 Geli-Putty® hemostatic gelatin unit Or 1 bottle of embolization microspheres Celonova</td>
</tr>
<tr>
<td>Other consumables</td>
<td>1 TERUMO Angled 0.032 guide 1 Cobra Small SF catheter 1 TERUMO SF short introducer 1 2-way HP tap 1 Progreat 2.7 TERUMO® micro-catheter</td>
</tr>
<tr>
<td>TOTAL</td>
<td>400.76 to 524.93</td>
</tr>
</tbody>
</table>

Unit price (U.P.). Excluding tax (ex. tax) extracted from the establishments tendering database. Quasi-routine use.
Affordability study

Affordability calculation: cost effectiveness was calculated using the following equation:

\[ \text{Affordability} = \text{SRG payment} - \text{Total cost of stay} \]

The total cost of the stay was the sum of the fixed and variable costs.

Calculation theoretical affordability

Theoretical affordability was calculated from the theoretical SRG payments set by the Decree of 27 February 2010 for the year 2010 according to the following equation [6]:

\[ \text{Theoretical affordability} = \text{Theoretical SRG 2010 payment} - \text{Total costs of stay} \]

Calculation of actual affordability

Actual affordability was calculated from the actual payments obtained from the DIM.

\[ \text{Actual affordability} = \text{Actual payment} - \text{Total cost of stay} \]

Affordability break-even point

The hypothesis used was based on defining a number of TACE procedures which could be performed in order to compensate for the average deficit due to a less cost-effective TACE-DEB procedure.

Results

Population

Thirty-one conventional TACE and 32 TACE-DEB courses were recorded in 2010.

Forty-nine of the procedures included or carried out in men and 14 in women. The sex ratio was uneven with 3.5 times more men than women treated. This is consistent with national epidemiological findings. The average age was 65 years old.

Patient distribution by DRG

Four DRG were involved (07M061, 07M062, 07M063, 07M064). The distribution of patients who underwent TACE or TACE-DEB according to the different DRG is shown below:

- DRG 07M061: 20 TACE, 26 TACE-DEB;
- DRG 07M062: 6 TACE, 4 TACE-DEB;
- DRG 07M063: 5 TACE, 1 TACE-DEB;
- DRG 07M064: 1 TACE-DEB.

Length of hospitalization

The average lengths of hospitalization for each DRG are listed in Table 3. When all of the DRGs were combined, there were no significant differences between the lengths of stay regardless of the embolization technique used.

Cost minimization analysis

The average total stay costs were used to make a financial comparison of the two types of chemo-embolization (Table 3).

When all of the DRG combined, the average cost of a TACE-DEB chemo-embolization was 3960.10 € compared to 2869.05 € for a TACE. This therefore represents an additional cost of 1091.05 €.

The embolization agents were responsible for the major additional cost of the difference between the average stay costs. The doxorubicin loaded embolization particles were responsible for an additional cost of 879.44 €. These particles alone therefore made up 25% of the total stay cost whereas the IMD for lipiodol chemo-embolization only represented 2% of the total stay cost.

The average cost of the other consumables for the TACE-DEB procedure was 77.20 € more than the cost of a TACE procedure.

Affordability study

The first comparison of theoretical affordability was carried out before considering actual affordability.

The sum of the theoretical affordability for each of the chemo-embolizations by DRG is shown in Fig. 1. Regardless of embolization type, the theoretical SRG tariff for DRG 07M061 does not cover the cost of chemo-embolization.

When the stay is included in DRGs 07M062 and 07M063, however, the conventional chemo-embolization technique (TACE) becomes cost-effective whereas the TACE-DEB technique remains in deficit. The TACE-DEB technique is only cost-effective when DRG 07M064 is used.

Analysis of the distribution of procedures by theoretical affordability and (Fig. 2) shows firstly that the conventional TACE technique is generally cost-effective in 64% of cases, compared to 13% for TACE-DEB technique. On the other hand, affordability is particularly negative for TACE-DEB, 47% of procedures result in a loss of over 1000 € compared
Table 3  Comparison of lengths of stay and all mean costs between conventional TACE and TACE-DEB.

<table>
<thead>
<tr>
<th>DRG</th>
<th>TACE conv.</th>
<th></th>
<th></th>
<th></th>
<th>TACE-DEB</th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean length of stay DMS (d)</td>
<td>Mean cost of stay (€)</td>
<td>Mean cost. IMD (€)</td>
<td>Mean cost of consumables (€)</td>
<td>Mean length of stay (d)</td>
<td>Mean cost of stay (€)</td>
<td>Mean cost of IMD (€)</td>
<td>Mean cost of consumables (€)</td>
</tr>
<tr>
<td>07M061</td>
<td>4.30</td>
<td>2801.24</td>
<td>86.01</td>
<td>365.02</td>
<td>4.23</td>
<td>3685.97</td>
<td>904.85</td>
<td>465.49</td>
</tr>
<tr>
<td>07M062</td>
<td>4.33</td>
<td>2436.38</td>
<td>13.52</td>
<td>408.91</td>
<td>9.25</td>
<td>5388.70</td>
<td>1102.39</td>
<td>390.80</td>
</tr>
<tr>
<td>07M063</td>
<td>8.00</td>
<td>3659.52</td>
<td>27.87</td>
<td>300.79</td>
<td>9.00</td>
<td>5628.41</td>
<td>1475.67</td>
<td>393.70</td>
</tr>
<tr>
<td>07M064</td>
<td>5.00</td>
<td>3704.79</td>
<td></td>
<td></td>
<td>5.00</td>
<td>3704.79</td>
<td>734.10</td>
<td>98.55</td>
</tr>
<tr>
<td>Mean of SRG and costs</td>
<td>4.90 ± 3.36</td>
<td>2869.05</td>
<td>62.60</td>
<td>365.24</td>
<td>5.03 ± 3.36</td>
<td>3960.10</td>
<td>942.04</td>
<td>442.44</td>
</tr>
</tbody>
</table>

Mean Length of Stay (DMS) and mean costs are expressed for each of the Diagnostic Reference Groups (DRG) included in this study. Lengths of stay were extracted from the healthcare software (Clinicom). The average cost of stay was assessed using the readjusted ENCC method. IMD and the consumable costs were determined by microcosting of reconstitution of the chemo-embolization particles. The mean of the DMS and the mean of the costs for all DRG by embolization technique were also calculated.
to 9% of TACE procedures. Therefore eighty-seven per cent of TACE-DEB chemo-embolization produce a deficit.

The actual payments may differ from the theoretical SRG payments, particularly when expensive compounds (doxorubicin) or IMD which are additionally reimbursed are required (none in this situation). These payments can also be influenced by the patient reimbursement rates. Data on actual affordability are shown in Figs. 3 and 4.

Unlike the theoretical affordability assessment, actual affordability can show whether the conventional technique is fundable regardless of the DRG, including DRG07M061 (Fig. 3). Overall, the TACE-DEB technique is also fundable regardless of DRG (Fig. 3).

An analysis of the distribution of procedures by positive or negative affordability (Fig. 4) over the study period shows that almost all of the conventional procedures are fundable (97%). Only one stay was found to have negative affordability of 0 to −500 € which is explained by high use of concomitant MD as the patient underwent parallel radio-frequency ablation in parts of the tumor (Fig. 4).

In terms of the TACE-DEB procedures, we can consider that half of these are fundable. Actual affordability of over 0 € is seen for 50% of patients treated with TACE-DEB (Fig. 4).

Affordability breakeven point

In order to be cost-effective, an average of at least 1.3 times more conventional TACE procedures needs to be performed than TACE-DEB. In reality in 2010, 75 conventional TACE procedures and 33 TACE-DEB procedures were carried out, i.e. 2.3 times more conventional TACE than TACE-DEB procedures, which leads us to assume that the establishment profited from the chemo-embolizations carried out in 2010.

Discussion

The chemo-embolization techniques proposed recently to treat patients suffering from non-metastatic, inoperable HCC are new techniques whose financial impact on healthcare establishments is poorly understood. The only randomized phase II study (PRECISION V study) which has been published to date comparing patients treated with conventional chemo-embolization (TACE) or chemo-embolization with loaded microspheres (TACE-DEB) showed no significant difference between the 2 procedures in terms of 6 month efficacy [3]. The medico-economic analysis, and particularly a cost minimization analysis, therefore appeared to be a useful tool for healthcare establishments in deciding on their strategic choices [4]. From this, our study has shown that a ratio of 1.3 procedures using the conventional method (TACE) should allow TACE-DEB procedures to be funded.

Our analysis of economic data showed a significantly higher additional stay cost for TACE-DEB compared to a conventional TACE stay (average 1091.05 €). These
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differences are explained by two main expenditure lines: firstly expenditure due to other consumables including non-implantable MD used during the embolization technique (catheter, guide, probe, micro-catheter). Micro-catheters (335.00 € per unit excluding tax.) are used almost routinely in TACE-DEB chemo-embolization whereas this is not the case with the TACE procedure. The second cost plan explaining the differences are the IMD made up of the embolization agents.

A comparison of actual and theoretical affordability shows that actual payments are on average 1.5 times greater than theoretical payments, therefore reducing the additional cost and increasing affordability. These differences can be explained by use of expensive molecules during the stay, which require additional reimbursement (particularly doxorubicin). These costs are incorporated into the actual payments by the Nantes University Hospitals convergence rate and by patient reimbursement rates given by the National Health Insurance Funds.

The theoretical payments were used in the subsequent assessment of loaded particles in order to be able to remove bias, particularly from differential patient reimbursement rates.

The theoretical affordability studies showed that only 13% of TACE-DEB procedures are cost-effective compared to 64% for conventional procedures. In order to examine how loaded microspheres could be fundable, a break-even affordability hypothesis was put forth. The two techniques for the procedures become fundable when they are used together in the ratio of 1.3 conventional TACE procedures to each TACE-DEB procedure. This involves patient selection and selection of disease severity so that its activity can be funded by the healthcare establishment.

This retrospective study has showed that the use of loaded particles has a genuine financial impact although the limitations of the study sample need to be considered. The study population was not matched, which reduces the power of the statistical tests, and in addition, low patient recruitment in the DRG of patients with high co-morbidities (DRG 07M063 and DRG 07M064) in the conventional TACE group makes it difficult to interpret and compare the two types of embolization. The cost minimization analysis which was carried out, however, does show an additional cost of chemo-embolization with loaded particles to treat HCC in the establishment over the year 2010. These results are consistent with those of another study which showed a significantly higher annual cost for TACE-DEB [8]. Another study has shown a lower overall cost for chemo-embolizations carried out using HepaSphere™ loaded microspheres (Biosphere Medical, South Jordan, USA) compared to conventional chemo-embolization. [9]. This reduction in cost was mostly due to the lower intrinsic cost of the HepaSphere™ compared to the DC-Bead™ used in our study. This study also only considered the first course of chemo-embolization and not all of the courses received by the patients suffering from HCC. In addition, patients recruited for chemo-embolization with HepaSphere™ had uni- or multifocal HCC and multifocal or diffuse HCC was treated with conventional chemo-embolization. These were therefore patients suffering from less severe HCC who were selected to receive chemo-embolization with HepaSphere™. Finally, this study was based on two different versions of the DRG classification (versions 10C and v11) which had fewer severity levels in the 10C version and resulted in a shift of patient classification, towards severer co-morbidities which were therefore better remunerated. Four levels of severity are listed in the current version. The reimbursement of patients with co-morbidities is financially lower (level 1 or 2) [10]. A study by the same group has recently been published [11] which examined the costs of TACE-DEB. The cost results from our study partially confirm those reported in this study. The study did not, however, support the potential self-funding of TACE-DEB by TACE as we have shown, particularly for some DRGs.

In addition to this cost analysis, this work shows that it is possible to fund the DC-Bead™ for DRG 07M064. Along the same lines as the studies discussed above [9,11], it would probably be useful to continue investigations with particular emphasis on this DRG. As the Precision V study [3] showed that DC-Bead™ laden particles offered a clinical benefit to patients suffering from advanced HCC this new approach would be particularly interesting. Future studies would also need to take into account the anesthetic resources which are more limited with the TACE-DEB technique, though this is only rarely considered, and also take account of the fact that patient tolerability is better for TACE-DEB than it is for the TACE technique.

Conclusion

This study highlights the difference which may exist between estimated hospital costs and the corresponding reimbursement amount for the hospital stay. This shows sustainable access to new surgical developments for each patient in a context of hospital deficit reduction and the desire for convergence between private and public healthcare establishments. This study has demonstrated that TACE-DEB procedures can be funded with a ratio of 1.3 to 1 (TACE/TACE-DEB).

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


