REVIEWER 1 :

1. The first and foremost, the efficacy of Idarubicin and Doxorubicin should be discussed. Do the two drugs have the same anticancer effect? The author should discuss it in the light of literature.

Answer: Thank you for this comment. This point is essential and very few data are available in literature and doxorubicin is the most commnly used without strong level of evidence (EASL guidelines. J Hepatol 2018). As discussed in both introduction and discussion, growing data suggest idarubicin as an interesting alternative (Boulin et al. Aliment Pharmacol Ther 2014 ; Guiu et al. J Hepatol 2018). Besides, in vitro data showed a much higher cytotoxicity of idarubicin compared with doxorubicin in tumor cells (Boulin et al. Anticancer Drugs 2011) with better chemical characteritics (Gallois et al. Biochimica et Biophysica Acta (BBA) - Biomembranes 1998)

2. The effect of c-TACE and DEB-TACE should be discussed respectively. Is there any difference?

Answer: Thank you for this remark. DEB-TACE did not show superiority compared to conventional TACE in several prospective comparative trials (Lammer et al. CVIR 2010 ; Varela et al. J Hepatol 2017 ; Golfieri et al. Br J Cancer 2014) . This technique is supposed to induce less liver toxicity but this was not clearly shown is literature and it induces more biliary complications due to more intense arterial ischemia. point is already explained in introduction concerning data from literature. We clarified this point in introduction.

Comparison of both techniques in our study was not an objective but as expected, due to small groups, and the absence of differences in larger prospective trials, no difference has been shown (unpublished data).

3.How many cases are c-TACE and DEB-TACE in the two groups respectively? Is the proportion balanced? Is there a difference of anticancer effect caused by imbalance of proportions?

Answer: This point is shown in table 1: same proportion of DEB-TACE is present in both groups: 12 patients (20%) and 6 patients (20%) in doxorubicin and idarubicin groups respectively. Consequently, this should not constitute a confusion bias.

4.The choice of the anticancer drugs used in TACE is still debated. The author should discuss this properly. Evidence or results of studies advocating the use of chemotherapeutic drugs; evidence or research findings advocating embolization only (with not anticancer drugs/not chemoembolization); and the possible reasons for these controversies.

Answer: Very few data are available in literature regarding the choice of chemotherapeutic drug. This point has been clarified in discussion with the adding of a reference (Boulin et al. Eur Radiol 2016) showing the better stability of idarubicin-based lipiodol emulsion. Embolisation versus chemoembolisation is another subject strongly debated with a low level of evidence. We developed this point regarding your comments.

5.How about the standard dose doxorubicin versus idarubicin, a dose thought to have equivalent anti-cancer activity?

Answer: Thank you for this question. Few data are available concerning optimal doxorubicin dose but the most common is 50mg in literature. We choosed a dose of 10 mg for idarubicin based on in vitro data and preliminary data from IDASPHERE phase 1 study that use idarubicin-eluting beads. Optimal dose of idarubicin in lipiodol-emulsion was not known at the time of this study, and a recent phase 1 study suggested the maximum tolerated dose of 20 mg (Guiu et al. J Hepatol 2018). We described this point in discussion as a limit of our study that may require a new prospective trial with 20 mg of idarubicin to obtain superior anti tumor efficacy.

6. Some sentences describing the results in this article are confusing, or not in conformity with the custom. Please check and modify them.

For example: Abstract section: There were 93 and 87% of cirrhotic patients and 87 and 70% of Child-Pugh A in Doxorubicin and Idarubicin groups, respectively. The median number of HCC per patient was 2 in both groups with 31and 26% of single nodules in Doxorubicin and Idarubicin groups. ORR after first TACE was 76.7% and 73.3% (p=0.797) with 41.7 and 40.0% complete response in Doxorubicin and Idarubicin groups, respectively.

Anti-tumor efficacy: Comparison of Dox-TACE and Ida-TACE section: Tumor response evaluation within 3 months post-TACE, according to mRECIST criteria, showed an ORR of 76% and 73% (p=0.797) with 41 and 40% of CR, and

36% and 33% of PR in Dox-TACE and Ida-TACE groups respectively. DCR was 90 and 87%, respectively (p=0.726) (Figure 2), etc. Partially marked. Plesae see marked.

Answer : Compatibility problem should occurred because all the correction marks concern lacking spaces between words that are not present on original manuscript.

7.The size of gelatin sponge particles, the dosage of lipiodol and gelatin sponge particles, and the criteria for stopping embolization should be described.

Answer: Thank you for this relevant critic. These informations have been added in method section.

REVIEWER 2 :

This paper is interesting. I recommend its potential publication in this journal. The first comment is about the study design. The authors said that they performed 90 patients treated with TACE for HCC, including 60 with Dox-TACE and 30 with Ida-TACE. And then they matched the two groups at a ratio of 2:1. It is confusing. How many patients with intermediate stage hepatocellular carcinoma performed TACE during the period? How did the authors selected the 90 patients form total patients? The information is very important for evaluating the bias of selection.

During this period, 155 patients underwent TACE with 30 patients who received idarubicin-TACE. We performed a matching as explained in the manuscript to obtain comparable groups of treatment and we did a 2:1 matching because of the larger number of doxorubicin TACE patients. This matching was performed blindly to efficacy or safety data to avoid any selection bias.

The language should be carefully improved. For example, "adverse events (AEs)" are repeatedly used. Please use abbreviations after the first time of full name. In the sentence "... TACE because cardiac rhythm disturbances", "of" should be added. "...in a bridge-to-transplant settings" should be revised. Other errors should be carefully checked.

Answer : This errors have been adressed.

Subheadings are useful for your Discussion section. I cannot see your figures and tables in the manuscript file.
Answer : This probem has been adressed

When the authors said "a recent randomized trial including 101 patients [19] suggested that transarterial embolization, also called bland embolization, offers comparable outcomes to TACE.", they should not neglect other evidence regarding TAE versus TACE. A recent overview of current evidence (v.) has summarized some meta-analyses and should be discussed.
Answer : Dear reviewer, it is true that this topic is controversial and we insisted on this point by suggesting that the effect of chemotherapeutic agent is probably mild and further trials with larger groups of patients are needed. The recent overview of the Management of hepatocellular carcinoma has been added to this discussion.

REVIEWER 3 :

1. Only single-center experience comparing TACE with Idarubicin versus TACE with Doxorubicin were ported. 2. Data were two old.
Answer: Dear reviewers, we believe that our data are of value because TACE methods did not changed during the last decade. Growing data showing idarubicin as an alternative to Doxorubicin habe been published in the last 5 years but only in single-arm trials studying Idarubicin. This study offers a comparison of both drugs in comparable groups based on patients' characteristics. The fact that every patient came from the same center also increases the comparability of the 2 different groups.