African Americans are less likely to receive curative treatment for hepatocellular carcinoma

Lindsay A Sobotka, Alice Hinton, Lanla F Conteh

AIM
To determine if racial disparities continue to exist in the treatment of hepatocellular carcinoma (HCC).

METHODS
A retrospective database analysis using the Nationwide Inpatient Sample was performed including patients with a primary diagnosis of HCC. Univariate and multivariate analyses were utilized to determine racial disparities in liver decompensation, treatment, inpatient mortality, and metastatic disease.

RESULTS
A total of 62604 patients with HCC were included consisting of 32428 Caucasian, 9726 African-American, 8988 Hispanic, and 11462 patients of other races. Caucasian patients were more likely to undergo curative therapies of liver transplant (OR: 2.66, 95%CI: 1.92-3.68), resection (OR: 1.82, 95%CI: 1.48-2.23), and ablation (OR: 1.77, 95%CI: 1.36-2.30) than African-American patients. Hispanic patients were more likely to undergo transplant (OR: 2.18, 95%CI: 1.40-3.39) and ablation (OR: 1.46, 95%CI: 1.02-2.13) than African-American patients. Other races were less likely to receive transplant (OR: 0.88, 95%CI: 0.72-1.07) and ablation (OR: 0.78, 95%CI: 0.60-1.01) compared to Caucasian patients.
Racial disparities in the treatment of hepatocellular carcinoma (HCC) have been noted previously. This study investigated continued disparities in healthcare utilizing the Nationwide Inpatient Sample. African-American patients were less likely to undergo curative treatments, such as liver transplantation, liver resection, ablation, and transarterial chemoablation for HCC despite having less features of liver decompensation.

**Key words:** Racial disparity; Hepatocellular carcinoma; Liver transplantation; Resection; Ablation

© The Author(s) 2018. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Racial disparities in the treatment of hepatocellular carcinoma (HCC) have been noted previously. This study investigated continued disparities in healthcare utilizing the Nationwide Inpatient Sample. African-American patients were less likely to undergo curative treatments, such as liver transplantation, liver resection, ablation, and transarterial chemoablation for HCC despite having less features of liver decompensation.

Sobotka LA, Hinton A, Conte LF. African Americans are less likely to receive curative treatment for hepatocellular carcinoma. *World J Hepatol* 2018; 10(11): 849-855 Available from: URL: http://www.wjgnet.com/1948-5182/full/v10/i11/849.htm DOI: http://dx.doi.org/10.4254/wjh.v10.i11.849

**INTRODUCTION**

The incidence of hepatocellular carcinoma (HCC) has increased about 50% since 2003[1,2]. An increasing incidence across all races and ethnic groups has been noted, however the incidence in African-American and Hispanic patients has had the largest increase over the past ten years[1]. The incidence of HCC is two times higher in African-American, American-Indian, Alaskan-Native, and Hispanic patients compared to Caucasian patients[2]. Unlike other malignancies such as prostate cancer, where despite increases in incidence, mortality has actually declined, we have seen a concurrent increase in the mortality of HCC as the incidence increases. The mortality rates are twice as high in African-American patients compared to Caucasian patients[2,3]. A recent study completed using the Surveillance, Epidemiology, and End Results (SEER) database showed the median overall survival of all patients with HCC was 11 mo. However, African-American patients had a significantly worse prognosis compared to Caucasian patients with only a nine-month survival rate[4].

Racial disparities in the treatment of HCC have been highlighted in previous studies. African-American patients who presented with localized disease were less likely to undergo curative therapy with liver transplantation, surgical resection, and ablation compared to Caucasian patients with the same tumor burden[5,6]. Previous studies have also noted that African-American patients were more likely to present with metastatic HCC at the time of diagnosis and were therefore no longer candidates for specific curative treatments[7].

This study aims to investigate continued disparities in the treatment of HCC. We hypothesize that racial disparities will continue to be present despite recent emphasis for equal treatment in healthcare.

**MATERIALS AND METHODS**

**Data source**

Utilizing the ( Nationwide) Inpatient Sample, which is part of the Healthcare Cost and Utilization Project (HCUP), we performed a retrospective database analysis. The HCUP is one of the largest publically available inpatient databases. Information obtained included primary and secondary diagnoses and procedures, patient demographics, expected payment source, total charges, discharge status, and length of stay[8]. This study is exempt from review from The Ohio State University Institutional Review Board because patient information is de-identified.

**Study sample**

Utilizing International Classification of Diseases, Ninth Revision, Clinical Modification codes, patient with a primary diagnosis of HCC (ICD-9 155.0) were included in this study. Patients were excluded if they were under the age of 18, or if they had a malignancy in the liver that was not hepatic in origin.

**Outcomes of interest**

Primary outcomes of interest included treatment disparities in HCC based on race, which was defined as Caucasian, African-American, Hispanic, or other. Specific treatments for HCC that were evaluated included liver transplantation, liver resection, ablation, and transarterial chemoablation (TACE). Secondary outcomes included differences in inpatient mortality, liver decompensation, and metastatic disease.

**Covariates**

Other variables evaluated included gender, age, insurance provider, region where treatment was received, etiology of cirrhosis, features of liver decompensation, metastatic disease, and comorbidities, defined by the Elixhauser Comorbidity (Table 1)[9]. Modification of the Elixhauser Comorbidity score was performed to exclude liver disease. Features of liver decompensation included ascites, jaundice, and hepatic encephalopathy as previously defined in other studies[10]. These variables...
were determined by the appropriate ICD-9 code.

**Statistical analysis**

Association between race and factors of interest were evaluated using chi square tests. Multivariate regression models were fit for the presence of metastatic HCC, liver decompensation, mortality, and treatment. Terms in each module were determined through backwards selection where hepatitis C, hepatitis B, alcohol, non-alcoholic steatohepatitis (NASH), primary sclerosing cholangitis, primary biliary cirrhosis, autoimmune liver disease, metastasis, Elixhauser comorbidity score, and treatment were eligible for inclusion where appropriate. Data was analyzed using SAS software (version 9.4).

**RESULTS**

**Demographics**

There were 62604 patients with a primary diagnosis of HCC included in this study. The majority of the patients were Caucasian (32428, 52%) followed by African American (9726, 16%), Hispanic (8988, 14%), and patients of other races (11462, 18%).

**Liver severity, metastatic HCC, and inpatient mortality**

Upon univariate analysis, features of liver decompensation were significantly different between races ($P < 0.001$) (Table 1). Multivariate analysis demonstrated that Caucasian and Hispanic patients were more likely to have decompensated liver disease than African-American patients [(OR: 1.16, 95%CI: 1.03-1.30), (OR: 1.28, 95%CI: 1.10-1.30)] (Table 2).

Univariate analysis concluded the presence of metastatic disease was significantly different between races ($P = 0.007$) (Table 1). Upon multivariate analysis, Caucasian patients were less likely to have metastatic disease then African-American patients with HCC (OR: 0.82, 95%CI: 0.71-0.94). There was no statistical difference between other races (Table 2).

Inpatient mortality was significantly different between races upon univariate analysis ($P = 0.017$) (Table 1). Upon multivariate analysis, Caucasian patients were less likely to have inpatient mortality compared to African-American patients (OR: 0.78, 95%CI: 0.65-0.93). There was no statistical difference between other races (Table 2).

**Inpatient treatment of HCC**

There was a significant difference in treatment between races in the univariate analysis ($P < 0.001$) (Table 1). Upon stepwise multivariate analysis, Caucasian, Hispanic, and patients of other races were more likely to undergo liver transplantation compared to African-American patients [(OR: 2.66, 95%CI: 1.92-3.68), (OR: 2.18, 95%CI: 1.40-3.39), (OR: 2.41, 95%CI: 1.62-3.61)]. Caucasian patients and patients of other races were also more likely to undergo surgical resection than African-American patients (OR: 1.82, 95%CI: 1.48-2.23), (OR: 1.79, 95%CI: 1.39-2.32). Caucasian, Hispanic, and patients of other races were more likely to undergo ablation compared to African-American patients (OR: 1.77, 95%CI: 1.36-2.30), (OR: 1.46, 95%CI: 1.05-2.03), (OR: 2.03, 95%CI: 1.47, 2.80)]. There was no significant difference in the rates of TACE between races (Table 3).

**DISCUSSION**

African-American patients are less likely to undergo curative treatments for HCC, and this study confirms that treatment disparities continue to exist despite efforts to reduce healthcare disparities. TACE was the only treatment without a disparity in utilization between races. TACE, however, is not considered to be curative for HCC. It is a means of controlling the malignancy and is often used to downstage tumor burden for liver transplantation or to keep tumor burden within transplant criteria. Differences in treatment exist despite African-American patients being less likely to present with decompensated disease compared to Caucasian patients. We know that patients whose disease is better compensated have a better tolerance of liver directed therapies for HCC. African-American patients have increased rates of metastatic disease and higher inpatient mortality. There are multiple factors that contribute to racial disparities in the management of HCC, including disease progression at time of diagnosis and social determinants of health. It is crucial to recognize these factors and their associations in order to formulate interventions to reduce racial disparities in treatment given the direct effect on patient survival and quality of life.

African-American patients are less likely to undergo curative treatments for HCC and many factors influence this disparity with the presence of metastatic disease being one major limitation to treatment[11]. African-American patients were more likely to have metastatic disease at the time of initial diagnosis[7]. This may be influenced by decreased HCC screening exams in African-American patients[12] and also by genetic differences between races. The presence of metastatic disease is not the only contributor to treatment discrepancies, however. Previous studies have found that African-American patients were less likely to undergo surgical treatment for HCC than Caucasian patients even when they presented with the same tumor burden and both groups were within Milan criteria[13].

Social factors, specifically the location in which patients receive therapy play a crucial role when considering treatment for patients with HCC. This study showed that the majority of African-American patients receive care in the Southern region of the United States, and patients living in the Southern United States are less likely to undergo curative therapies of liver transplantation and surgical resection[14,15]. Decreased access to providers who are able to provide timely diagnosis and treatment contributes to this disparity because of the increased rates of physician and hospital bed inequality in the South compared to the North. This makes it more challenging for patients in these areas...
to access a Hepatologist and a hospital that is better equipped to meet their needs.\(^\text{[16]}\)

Racial disparities in the utilization of TACE was not noted in this study, though previous studies have determined a discrepancy in Native-American patients and Hispanic patients compared to Caucasian patients.\(^\text{[17]}\) This intervention may be considered more frequently in African-American patients compared to Caucasian patients. It is often noted that TACE is not considered curative therapy for many African-American patients. However, it should be noted that TACE is not considered curative therapy for HCC. The question of whether it is being offered as the sole treatment option for patients who would otherwise be candidates for curative therapy should be raised.

The cost of intervention also influences treatment options. This study shows that African-American patients are the largest percentage of patients with Medicaid insurance compared to other races. Previous analysis on

or multifocal HCC\(^\text{[18]}\) and may be the ideal treatment for many African-American patients. However, it should be noted that TACE is not considered curative therapy for HCC. The question of whether it is being offered as the sole treatment option for patients who would otherwise be candidates for curative therapy should be raised.

The cost of intervention also influences treatment options. This study shows that African-American patients are the largest percentage of patients with Medicaid insurance compared to other races. Previous analysis on
The cost of intervention for HCC has shown TACE to be one of the least costly interventions\(^1\), and therefore may be the intervention most likely to be reimbursed from government funded insurance.

While it is important to recognize racial disparities in the treatment of patients with HCC, it is crucial to recognize the effect this has on an underrepresented patient’s quality of life and life expectancy. Studies regarding quality of life in patients with chronic liver disease show decreased functional status and increased chronic, debilitating symptoms such as pain, edema, weakness, anorexia, and vomiting compared to patients without any liver disease\(^2\). These symptoms, specifically bodily pain and fatigue, are worse in patients with liver disease and HCC\(^3\). Patients with HCC are noted to have higher rates of depression compared to many other malignancies\(^4\); therefore African-American patients with HCC that fail to undergo treatment are subject to increased complications and diminished quality of life compared to patients that undergo treatment.

Life expectancy is also different between patients that undergo treatment for HCC compared to patients that are not treated\(^5\). If a patient were to undergo treatment, life expectancy and quality of life are improved\(^6,7\).

Multiple interventions could be utilized to reduce disparities in the treatment of HCC. For example, early recognition of liver disease and risk factors for HCC are key to initiate and continue HCC screening in all patients, but specifically in minority patients that may have reduced access to care. This could potentially lead to earlier diagnosis in patients, and therefore the patient would be a candidate for curative treatment.

Limitations in this study must be noted. This data was obtained through the NIS database through ICD-9 coding. Verification of ICD-9 codes could not be obtained for each patient included in the study given patient privacy restrictions. However, these codes have been verified in previous studies. Other factors, specifically

### Table 2 Multivariate logistic regressions comparing outcomes of hepatocellular carcinoma by race

| Outcome                  | Race          | Adjusted odds ratio | 95%CI        |
|--------------------------|---------------|---------------------|--------------|
| Metastatic Hepatocellular Carcinoma\(^1\) | African-American | Reference           |              |
|                          | Caucasian     | 0.82                | 0.71-0.94    |
|                          | Hispanic      | 0.87                | 0.73-1.05    |
|                          | Other/unknown | 0.84                | 0.70-1.001   |
| Liver Decompensation\(^2\) | African-American | Reference           |              |
|                          | Caucasian     | 1.16                | 1.03-1.30    |
|                          | Hispanic      | 1.28                | 1.10-1.51    |
|                          | Other/unknown | 1.14                | 0.995-1.31   |
| Inpatient Mortality\(^3\) | African-American | Reference           |              |
|                          | Caucasian     | 0.78                | 0.65-0.93    |
|                          | Hispanic      | 0.82                | 0.66-1.03    |
|                          | Other/unknown | 0.86                | 0.69-1.07    |

1\(^1\)Model is adjusted for age, sex, race, geographic region, hepatitis C, alcohol, non-alcoholic steatohepatitis (NASH), liver decompensation features, and Elixhauser comorbidity score; 2\(^2\)Model is adjusted for age, sex, race, geographic region, hepatitis C, alcohol, NASH, primary biliary cirrhosis, metastasis, and Elixhauser comorbidity score; 3\(^3\)Model is adjusted for age, sex, race, geographic region hepatitis C, hepatitis B, alcohol, NASH, liver decompensation features, metastasis, and treatment.

### Table 3 Multinomial logistic regression to evaluate disparities in treatment for hepatocellular carcinoma based on payer\(^1,2\)

| Intervention   | Race          | Odds ratio | Confidence interval |
|----------------|---------------|------------|---------------------|
| Liver Transplant | African-American | Reference |                    |
|                 | Caucasian     | 2.66       | 1.92-3.68           |
|                 | Hispanic      | 2.18       | 1.40-3.39           |
|                 | Other/unknown | 2.41       | 1.62-3.61           |
| Resection       | African-American | Reference |                    |
|                 | Caucasian     | 1.82       | 1.48-2.23           |
|                 | Hispanic      | 1.24       | 0.94-1.64           |
|                 | Other/unknown | 1.79       | 1.39-2.32           |
| Ablation        | African-American | Reference |                    |
|                 | Caucasian     | 1.77       | 1.36-2.30           |
|                 | Hispanic      | 1.46       | 1.05-2.03           |
|                 | Other/unknown | 2.03       | 1.47-2.80           |
| TACE            | African-American | Reference |                    |
|                 | Caucasian     | 1.15       | 0.93-1.41           |
|                 | Hispanic      | 1.29       | 0.97-1.72           |
|                 | Other/unknown | 1.39       | 0.90-1.58           |

1\(^1\)Noninvasive treatment is treated as the reference category; 2\(^2\)Model adjusts for age, gender, race, geographic region, hepatitis C, hepatitis B, alcohol, non-alcoholic steatohepatitis, liver decompensation features, and Elixhauser comorbidity score. TACE: Transarterial chemoablation.
size and number of lesions that affect the treatment for HCC were not included in this study. We were not able to obtain laboratory values and were unable to determine MELD score. Therefore, disease severity was defined by features of liver decompensation. Despite limitations, this study has several strengths. The primary strength was the number of patients that were enrolled in the study over a wide geographic area. Using the NIS database allowed for the collection of a large number of patients that otherwise would not have been obtained in a single institution study.

Disparities in the treatment of HCC based on patient race continue to exist despite emphasis to decrease disparities in healthcare. Despite having decreased rates of liver decompensation, African-American patient have higher rates of inpatient mortality and are less likely to undergo curative treatments, such as liver transplantation, surgical resection, or ablation. Because these patients are less likely to undergo these interventions, African-American patients with HCC are prone to a decreased quality of life and increased mortality rates. Further research needs to be conducted to find ways to decrease this disparity.

**ARTICLE HIGHLIGHTS**

**Research background**
Rates of hepatocellular carcinoma (HCC) continue to increase. Despite new treatment options, mortality rates are also increasing specifically in minority patients.

**Research motivation**
Given recent emphasis to minimize health care disparities, we aimed to determine if racial disparities in the treatment of HCC were decreasing.

**Research methods**
We performed a retrospective database analysis utilizing The Nationwide Inpatient Sample including patients with a diagnosis of HCC. Univariate and multivariate analyses were utilized to determine racial disparities in liver decompensation, treatment, inpatient mortality, and metastatic disease.

**Research results**
This large database analysis included 62,604 patients with HCC, including 32,428 Caucasian, 9,726 African-American, 9,898 Hispanic, and 11,462 patients of other races. Despite having decreased rates of liver decompensation, African-American patient have higher rates of inpatient mortality and are less likely to undergo curative treatments, such as liver transplantation, surgical resection, or ablation than Caucasian patients.

**Research conclusions**
Racial disparities in HCC treatment exist despite emphasis to support equality in healthcare. African-American patients are less likely to undergo curative treatments for HCC.

**Research perspectives**
Further emphasis should be placed on determining why disparities continue to exist and hypothesize ways to reduce them in order to facilitate equality in healthcare.

**REFERENCES**

1. Mittal S, El-Serag HB. Epidemiology of hepatocellular carcinoma: consider the population. *J Clin Gastroenterol* 2013; 47 Suppl: S2-S6 [PMID: 23632345 DOI: 10.1097/MCG.0b013e318287f2c9]
2. American Cancer Society. Atlanta: American Cancer Society, 2016
3. Nguyen GC, Thuluvath PJ. Racial disparity in liver disease: Biological, cultural, or socioeconomic factors. *Hepatology* 2008; 47: 1058-1066 [PMID: 18302296 DOI: 10.1002/hep.22223]
4. Xu L, Kim Y, Spolverato G, Gani F, Pawlik TM. Racial disparities in treatment and survival of patients with hepatocellular carcinoma in the United States. *Hepatobiliary Surg Nutr* 2016; 5: 43-52 [PMID: 26904556 DOI: 10.3978/j.issn.2304-3881.2015.08.05]
5. Crissien AM, Fresnet C. Current management of hepatocellular carcinoma. *Gastroenterol Hepatol (NY)* 2014; 10: 153-161 [PMID: 24829542]
6. Zak Y, Rhoads KF, Visser BC. Predictors of surgical intervention for hepatocellular carcinoma: race, socioeconomic status, and hospital type. *Arch Surg* 2011; 146: 778-784 [PMID: 21422327 DOI: 10.1001/archsur.2011.37]
7. Sloane D, Chen H, Howell C. Racial disparity in primary hepatocellular carcinoma: tumor stage at presentation, surgical treatment and survival. *J Natl Med Assoc* 2006; 98: 1934-1939 [PMID: 17225837]
8. Overview of the National (Nationale) Inpatient Sample (NIS). [Accessed 2016 March 31]. Available from: URL: https://www.hcup-us.ahrq.gov/nisoverview.jsp
9. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* 1998; 36: 8-27 [PMID: 9431328 DOI: 10.1097/00005650-199810000-00004]
10. Cauble S, Abbas A, Balart L, Bazzano L, Medvedev S, Shores N. United States women receive more curative treatment for hepatocellular carcinoma than men. *Dig Dis Sci* 2013; 58: 2817-2825 [PMID: 23812858 DOI: 10.1007/s10620-013-2731-9]
11. Soriano A, Arona A, Gianchandani R, Moneva ME, Arranz J, Gonzalez A, Barrera M. Selection of patients with hepatocellular carcinoma for liver transplantation: Past and future. *World J Hepatol* 2016; 8: 58-68 [PMID: 26783421 DOI: 10.4254/wjhl.v8.i1.58]
12. Harlan LC, Parsons HM, Wiggins CL, Stevens JL, Patt YZ. Treatment of hepatocellular carcinoma in the community: disparities in standard therapy, *Liver Cancer* 2015; 4: 70-83 [PMID: 26020030 DOI: 10.1159/000367729]
13. Artiyan A, Mailey B, Sanchez-Luenges N, Khalili J, Sun CL, Bhatia S, Wagman LD, Nissen N, Colquhoun SD, Kim J. Race, ethnicity, and socioeconomic status influence the survival of patients with hepatocellular carcinoma in the United States. *Cancer* 2010; 116: 1367-1377 [PMID: 20101732 DOI: 10.1002/cncr.24817]
14. Artiga S, Danico A. Health and health coverage in the south: A data update. [accessed 2016 February 10]. Available from: URL: http://kff.org/disparities-policy/issue-brief/health-and-health-coverage-in-the-south-a-data-update/
15. Rana A, Kaplan B, Riaz IB, Porubsky M, Habib S, Rilo H, Gruessner AC, Gruessner RW. Geographic inequities in liver allograft supply and demand: does it affect patient outcomes? *Transplantation* 2015; 99: 515-520 [PMID: 25700168 DOI: 10.1097/TP.0000000000000372]
16. Horev T, Pesis-Katz I, Mukamel DB. Trends in geographic disparities in allocation of health care resources in the US. *Health Policy* 2004; 68: 223-232 [PMID: 15063021 DOI: 10.1016/j.healthpol.2003.09.011]
17. Alkhaliili E, Greenbaum A, Luo L, Rodriguez R, Munoz OE, O’Neill J, Nir I, Morris KT. Racial disparities in treatment and survival of hepatocellular carcinoma in native Americans and Hispanics. *Am J Surg* 2017; 214: 100-104 [PMID: 28624027 DOI: 10.1016/j.amjsurg.2016.09.033]
18. Bruijs J, Sherman M. American Association for the Study of Liver Diseases. Management of hepatocellular carcinoma: an update. *Hepatology* 2011; 53: 1020-1022 [PMID: 21374666 DOI: 10.1002/hep.24199]
19. Ray CE Jr, Battaglia C, Libby AM, Prochazka A, Xu S, Funaki B.
Interventional radiologic treatment of hepatocellular carcinoma—a cost analysis from the payer perspective. J Vasc Interv Radiol 2012; 23: 306-314 [PMID: 22277271 DOI: 10.1016/j.jvir.2011.11.016]

20 Sun VC, Sarna L. Symptom management in hepatocellular carcinoma. Clin J Oncol Nurs 2008; 12: 759-766 [PMID: 18842532 DOI: 10.1188/08.CJON.759-766]

21 Bianchi G, Loguerco C, Sgarbi D, Abbiati R, Brunetti N, De Simone T, Zoli M, Marchesini G. Reduced quality of life of patients with hepatocellular carcinoma. Dig Liver Dis 2003; 35: 46-54 [PMID: 12725608 DOI: 10.1016/S1590-8658(02)00011-7]

22 Zabora J, BritzenhofeSzoc K, Curbow B, Hooker C, Piantadosi S. The prevalence of psychological distress by cancer site. Psychooncology 2001; 10: 19-28 [PMID: 11180574 DOI: 10.1002/1099-1611(200101/02)10:1<19::AID-PON501>3.0.CO;2-6]

23 Schneider H. Special problems in the use of respirators in the anesthesia of newborn infants and small children. Anaesthesist 1966; 15: 118-120 [PMID: 5234419 DOI: 10.1002/hep.27443]

24 Poon RT, Fan ST, Yu WC, Lam BK, Chan FY, Wong J. A prospective longitudinal study of quality of life after resection of hepatocellular carcinoma. Arch Surg 2001; 136: 693-699 [PMID: 11387012 DOI: 10.1001/archsurg.136.6.693]

25 Eltawil KM, Berry R, Abdolell M, Molinari M. Quality of life and survival analysis of patients undergoing transarterial chemoembolization for primary hepatic malignancies: a prospective cohort study. HPB (Oxford) 2012; 14: 341-350 [PMID: 22487072 DOI: 10.1111/j.1477-2578.2012.00455.x]

Sobotka LA et al. African Americans are less likely to receive curative treatment for HCC

P- Reviewer: Bramhall S, Chiu KW, Kinoshita A, Niu ZS, Tomizawa M
S- Editor: Cui LJ  L- Editor: Filipodia  E- Editor: Bian YN
