



**A Comparative Study of the Diagnostic and Prognostic Value of Macrophage Activation Marker Soluble CD163 and Alpha Fetoprotein in Cirrhotic Patients with Hepatitis C Virus-related Hepatocellular Carcinoma treated by Loco-Regional Therapy**

Thesis

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وَقُلْ اَعْمَلُوا فَسَيَرَى اللَّهُ  
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# List of Abbreviations

Abb.	Full term
<i>5`-NPD.....</i>	<i>5`-Nucleotide phosphodiesterase</i>
<i>AASLD.....</i>	<i>American Association for the Study of Liver Diseases</i>
<i>ADAM 17-TACE.....</i>	<i>ADMN metalloproteinase domain 17-tumor necrosis factor-<math>\alpha</math>-converting enzyme)</i>
<i>AFP.....</i>	<i>Alpha-Feto Protein</i>
<i>AFP-L3 .....</i>	<i>Lens culinaris agglutinin- reactive alpha-fetoprotein</i>
<i>AFU .....</i>	<i>Alpha L-Fucosidase</i>
<i>AJCC.....</i>	<i>American Joint Committee on Cancer</i>
<i>ALP.....</i>	<i>Alkaline phosphatase</i>
<i>ALT .....</i>	<i>Alanine Aminotransferase</i>
<i>ART.....</i>	<i>Anti-retroviral therapy</i>
<i>AST .....</i>	<i>Aspartate Aminotransferase</i>
<i>AUC .....</i>	<i>Area under curve</i>
<i>BCLC.....</i>	<i>Barcelona-Clinic Liver Cancer</i>
<i>BSC.....</i>	<i>Best Supportive Care</i>
<i>CBP.....</i>	<i>Child bearing period</i>
<i>CCL22.....</i>	<i>C-C motif chemokine 22</i>
<i>CD163.....</i>	<i>Cluster of Differentiation 163</i>
<i>CDC .....</i>	<i>Centers for Disease Control</i>
<i>CEA.....</i>	<i>Carcinoembryonic Antigen</i>
<i>CEUS.....</i>	<i>Contrast enhanced ultrasound</i>
<i>CI .....</i>	<i>Confidence Interval</i>
<i>CKD .....</i>	<i>Chronic Kidney Disease</i>
<i>CLD.....</i>	<i>Chronic liver disease</i>
<i>CLIP.....</i>	<i>Cancer of the Liver Italian Program</i>

# List of Abbreviations cont...

Abb.	Full term
<i>CR</i> .....	<i>Complete response</i>
<i>CSF</i> .....	<i>Colony stimulating factor</i>
<i>CT</i> .....	<i>Computed tomography</i>
<i>CUPI</i> .....	<i>Chinese University Prognostic Index</i>
<i>DAAs</i> .....	<i>Direct Acting Antivirals</i>
<i>DAC</i> .....	<i>Daclatasvir</i>
<i>DCP</i> .....	<i>Des-gamma carboxyprothrombin</i>
<i>DDIs</i> .....	<i>Drug drug interactions</i>
<i>DM</i> .....	<i>Diabetes mellitus</i>
<i>DMSA</i> .....	<i>Dimercaptosuccinic acid</i>
<i>DNA</i> .....	<i>Deoxyribonucleic acid</i>
<i>DWI</i> .....	<i>Diffusion-weighted</i>
<i>EASL</i> .....	<i>European Association for the Study of the Liver</i>
<i>ECOG</i> .....	<i>Eastern Cooperative Oncology Group</i>
<i>EDHS</i> .....	<i>Egyptian Demographic Health Survey</i>
<i>eGFR</i> .....	<i>Estimated glomerular filtration rate</i>
<i>EHIS</i> .....	<i>Egyptian Health Issues Survey</i>
<i>EIA</i> .....	<i>Enzyme immunoassay</i>
<i>ELISA</i> .....	<i>Enzyme linked immunosorbent assay</i>
<i>EORTC</i> .....	<i>European Organisation for Research and Treatment of Cancer</i>
<i>EPO</i> .....	<i>Erythropoietin</i>
<i>ER</i> .....	<i>Endoplasmic Reticulum</i>
<i>ESCRT</i> .....	<i>Endosomal-Sorting Complex Required for Transport</i>
<i>ESLC</i> .....	<i>Egyptian Society of Liver Cancer</i>
<i>EU</i> .....	<i>European Union</i>

## List of Abbreviations cont...

Abb.	Full term
<i>EUS</i> .....	<i>Endoscopic ultrasound</i>
<i>FE</i> .....	<i>Fisher Exact</i>
<i>GPC3</i> .....	<i>Glypican-3</i>
<i>HBsAg</i> .....	<i>Hepatitis B Virus surface Antigen</i>
<i>HBV</i> .....	<i>Hepatitis B virus</i>
<i>HCC</i> .....	<i>Hepatocellular Carcinoma</i>
<i>HCV</i> .....	<i>Hepatitis C virus</i>
<i>HRP</i> .....	<i>Horseradish peroxidase</i>
<i>HSP</i> .....	<i>Heat shock protein</i>
<i>HTERT</i> .....	<i>Human telomerase reverse transcriptase mRNA</i>
<i>ICC</i> .....	<i>Intrahepatic cholangiocarcinoma</i>
<i>IDSA</i> .....	<i>Infectious Diseases Society of America</i>
<i>IFN</i> .....	<i>Interferone</i>
<i>IGF II</i> .....	<i>Insulin like growth factor 2</i>
<i>IL-8</i> .....	<i>Interleukin-8</i>
<i>INR</i> .....	<i>International normalized ratio</i>
<i>IOUS</i> .....	<i>Intraoperative ultrasound</i>
<i>ISDR</i> .....	<i>Interferon Sensitivity Determining Region</i>
<i>IU</i> .....	<i>International units</i>
<i>JIS</i> .....	<i>Japan Integrated Staging</i>
<i>JSH</i> .....	<i>Japan Society of Hepatology</i>
<i>KDa</i> .....	<i>Kilodalton</i>
<i>LA</i> .....	<i>Laser ablation</i>
<i>LDLT</i> .....	<i>Living Donor Liver Transplant</i>
<i>LED</i> .....	<i>Ledipasvir</i>
<i>LI-RADS</i> .....	<i>Liver imaging reporting and data system</i>
<i>LPS</i> .....	<i>Lipopolysaccharide</i>

# List of Abbreviations cont...

Abb.	Full term
<i>LRT</i> .....	<i>Locoregional therapy</i>
<i>LT</i> .....	<i>Liver Transplantation</i>
<i>MAGE</i> .....	<i>Melanoma antigen gene</i>
<i>MC</i> .....	<i>Monte Carlo</i>
<i>MCT</i> .....	<i>Microwave coagulation therapy</i>
<i>MELD</i> .....	<i>Model for End-stage liver Disease</i>
<i>MMP</i> .....	<i>Matrix metalloproteinase</i>
<i>MRI</i> .....	<i>Magnetic resonance imaging</i>
<i>MSM</i> .....	<i>Men who have sex with men</i>
<i>NAFLD</i> .....	<i>Nonalcoholic fatty liver disease</i>
<i>NASH</i> .....	<i>Nonalcoholic steatohepatitis</i>
<i>NAT</i> .....	<i>Nucleic acid testing</i>
<i>NHL</i> .....	<i>Non Hodgkin lymphoma</i>
<i>NNPIs</i> .....	<i>Non-nucleoside polymerase inhibitors</i>
<i>NTRs</i> .....	<i>Non-Translated Regions</i>
<i>OPTN</i> .....	<i>Organ Procurement and Transplantation Network</i>
<i>ORF</i> .....	<i>Open Reading Frame</i>
<i>OS</i> .....	<i>Overall survival</i>
<i>OST</i> .....	<i>Opioid substitution therapy</i>
<i>PAL</i> .....	<i>Percutaneous Acetic Acid Injection</i>
<i>PCR</i> .....	<i>Polymerase chain reaction</i>
<i>PDGFR</i> .....	<i>platelet-derived growth factor receptor</i>
<i>PEI</i> .....	<i>Percutaneous Chemical Ablation</i>
<i>PEI</i> .....	<i>Percutaneous ethanol injection</i>
<i>PET</i> .....	<i>Positron emission tomography</i>
<i>PMA</i> .....	<i>phorbol myristate acetate</i>

# List of Abbreviations cont...

Abb.	Full term
<i>PS</i> .....	<i>Performance State</i>
<i>PT</i> .....	<i>Prothrombin time</i>
<i>PVT</i> .....	<i>Portal vein thrombosis</i>
<i>PWID</i> .....	<i>People who inject drugs</i>
<i>RBV</i> .....	<i>Ribavirin</i>
<i>RCT</i> .....	<i>Randomized control trial</i>
<i>RDTs</i> .....	<i>Rapid diagnostic tests</i>
<i>RFA</i> .....	<i>Radiofrequency Ablation</i>
<i>RNA</i> .....	<i>Ribonucleic acid</i>
<i>ROC</i> .....	<i>Receiver operating characteristic</i>
<i>ROS</i> .....	<i>Reactive Oxygen Species</i>
<i>SCCA</i> .....	<i>Serum squamous cell carcinoma antigen</i>
<i>sCD163</i> .....	<i>Soluble CD163</i>
<i>SD</i> .....	<i>Standard deviation</i>
<i>SHARP</i> .....	<i>Sorafenib Hepatocellular Carcinoma Assessment Randomized Protocol</i>
<i>SIM</i> .....	<i>Simeprevir</i>
<i>SOF</i> .....	<i>Sofosbuvir</i>
<i>SRB 1</i> .....	<i>Scavenger Receptor B1</i>
<i>SRCR</i> .....	<i>Scavenger receptor cysteine-rich</i>
<i>STAT</i> .....	<i>Signal transducer and activator of transcription</i>
<i>SVR</i> .....	<i>Sustained Virological Response</i>
<i>TACE</i> .....	<i>Transcatheter arterial chemoembolization</i>
<i>TACE-DEB</i> .....	<i>Chemoembolization with Drug-Eluting Beads</i>
<i>TAE</i> .....	<i>Transarterial embolization</i>
<i>TAMs</i> .....	<i>Tumor-associated macrophages</i>

## List of Abbreviations cont...

Abb.	Full term
<i>TARE</i> .....	<i>Transarterial radioembolization</i>
<i>TGF-beta</i> .....	<i>Transforming Growth Factor beta</i>
<i>TLR</i> .....	<i>Toll-like receptor</i>
<i>TNF</i> .....	<i>Tumor necrosis factor</i>
<i>TNM</i> .....	<i>Tumor, node, and metastases</i>
<i>TNM</i> .....	<i>Tumor-Node-Metastasis Staging System</i>
<i>UCSF</i> .....	<i>University of California, San Francisco criteria</i>
<i>UICC</i> .....	<i>Union International Contre le Cancer.</i>
<i>US</i> .....	<i>Ultrasound</i>
<i>USA</i> .....	<i>United states of America</i>
<i>VEGF</i> .....	<i>Vascular endothelial growth factor</i>
<i>VEGFR</i> .....	<i>Vascular endothelial growth factor receptor</i>
<i>VIP</i> .....	<i>Vasoactive Intestinal peptide</i>
<i>WHO</i> .....	<i>World Health Organization</i>

## ABSTRACT

**Background:** hepatocellular carcinoma (HCC) shows an increasing incidence and represents the third most common cause of cancer-related death.

**Aim of the Work:** is to evaluate the diagnostic value of serum level of Macrophage activation marker soluble CD163 as a tumor marker for HCC and its prognostic value after transarterial chemo-embolization (TACE) or radiofrequency ablation (RFA), in comparison to alpha-feto protein (AFP).

**Patients and Methods:** this study was performed on 60 subjects from the outpatient Hepatology clinic and inpatient Gastroenterology and Hepatology Department at Ain Shams University Hospital. **Group I:** includes 40 randomly selected cirrhotic patients with hepatitis C virus-related hepatocellular carcinoma (excluding BCLC class D) who underwent either RFA or TACE. **Group II:** includes 20 patients with liver cirrhosis without hepatocellular carcinoma considered as control.

**Results:** soluble CD163 expression did not differ significantly between HCC group and liver cirrhosis group. This proves that soluble CD163 is not suitable for diagnostic use. On the other hand, soluble CD163 was associated with the severity of liver disease. Baseline soluble CD163 was significantly associated with disease progression independent of other risk factors known to be associated with an unfavorable course in HCC. Also the marked significant reduction of serum soluble CD163 levels in HCC patients subjected to either RF ablation or TACE proved that soluble CD163 may play a prognostic marker in HCC monitoring.

**Conclusion:** soluble CD163 is not suitable as a diagnostic marker for HCC but can be used as a prognostic marker for HCC.

**Keywords:** Macrophage Activation Marker Soluble CD163, Alpha Fetoprotein in Cirrhotic, Hepatitis C Virus, Hepatocellular Carcinoma, Loco-Regional Therapy