

Persistent Inflammation, Immunosuppression Catabolism Syndrome

Subjects: [Pathology](#) | [Nutrition & Dietetics](#)

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Combining new immunological insights with great clinical experience is how the Persistent Inflammation, Immunosuppression and Catabolism Syndrome (PICS) was first described in 2012 [1]. The attempt to translate fundamental research into readily available surrogates in order to describe a clinical condition is how biomarkers and their cut-offs were determined. In the recent past, PICS has more and more become an acknowledged concept regarding ICU patients on their transition to chronic critical illness.

[PICS](#)[MDSC](#)[DAMPs](#)[inflammation](#)[immunosuppression](#)

1. Introduction

Since its first description by Gentile et al. in 2012^[1], the concept of PICS has been validated and is becoming more and more accepted as the underlying pathophysiology of chronic critical illness (CCI)^{[2][3][4][5][6][7][8]}.

2. Clinical Markers

The paradigm implies that, following the simultaneously triggered pro- and anti-inflammatory responses to a major inflammatory insult (e.g. trauma, burns, sepsis, acute pancreatitis, etc.) the increasing number of acute survivors either proceed to a fairly rapid recovery or a prolonged trajectory partially ending in CCI^{[2][3]}. Clinically spoken these patients present with a prolonged ICU stay (typically > 14 days) under the coexistence of ongoing inflammation and immunosuppression resulting in persistent catabolism and organ dysfunction^{[2][3][4]}. Besides an ICU length of stay (LOS) of over 14 days, applied clinical markers defining the diagnosis are a c-reactive protein (CRP) over 0.15 mg/dl as sign of inflammation, a total lymphocyte count under 0.800 G/l as sign of immunosuppression and a serum albumin concentration under 3.0 g/dl, a creatinine height index under 80% or a weight loss over 10% as signs of ongoing catabolism^[1]. Regarding sepsis patients on a surgical ICU an observational study was able to show that more than half of the acute survivors ended up developing CCI. This was associated with an older age, an increased rate of hospital acquired infections and a 6-month survival of merely 63%^[9]. On a cellular level initial emergency myelopoiesis also induces a primarily beneficial expansion of so-called myeloid-derived suppressor cells (MDSC)^{[10][11]}. However, a prolonged expansion of these MDSCs promotes the suppression of adaptive immunity and the evolvement of chronic inflammation^{[12][13][14]}. The concomitant tissue damage of trauma, major surgery or sepsis with the release of damage associate molecular patterns (DAMPs) can amplify the above

mentioned^{[15][16]}. Even mere muscle wasting – itself triggered by the ongoing inflammation – has been shown to propagate systemic inflammation through liberation of mitochondria derived DAMPs^{[17][18]}. Monocyte paralysis with reduced phagocytosis and HLA-DR expression as well as a reduced T-cell proliferation with elevated expression of suppressor molecules (e.g. programmed death ligand – 1; PDL-1) are only a few of the known inhibitory results, lastly predisposing for recurrent infections and therefore feeding this viscous cycle^{[4][9][19][20]}.

References

1. Gentile, L.F.; Cuenca, A.G.; Efron, P.A.; Ang, D.; Bihorac, A.; McKinley, B.A.; Moldawer, L.L.; Moore, F.A. Persistent inflammation and immunosuppression. *J. Trauma Acute Care Surg.* 2012, 72, 1491–1501, doi:10.1097/ta.0b013e318256e000.
2. Mira, J.C.; Brakenridge, S.C.; Moldawer, L.L.; Moore, F.A. Persistent Inflammation, Immunosuppression and Catabolism Syndrome. *Crit. Care Clin.* 2017, 33, 245–258, doi:10.1016/j.ccc.2016.12.001.
3. Efron, P.A.; Mohr, A.M.; Bihorac, A.; Horiguchi, H.; Hollen, M.K.; Segal, M.S.; Baker, H.V.; Leeuwenburgh, C.; Moldawer, L.L.; Moore, F.A.; et al. Persistent inflammation, immunosuppression, and catabolism and the development of chronic critical illness after surgery. *Surgery* 2018, 164, 178–184, doi:10.1016/j.surg.2018.04.011.
4. Hawkins, R.B.; Raymond, S.L.; Stortz, J.A.; Horiguchi, H.; Brakenridge, S.C.; Gardner, A.; Efron, P.A.; Bihorac, A.; Segal, M.; Moore, F.A.; et al. Chronic Critical Illness and the Persistent Inflammation, Immunosuppression, and Catabolism Syndrome. *Front. Immunol.* 2018, 9, 1511, doi:10.3389/fimmu.2018.01511.
5. Hesselink, L.; Hoepelman, R.J.; Spijkerman, R.; Groot, M.C.H. de; Wessem, K.J.P. van; Koenderman, L.; Leenen, L.P.H.; Hietbrink, F. Persistent Inflammation, Immunosuppression and Catabolism Syndrome (PICS) after Polytrauma: A Rare Syndrome with Major Consequences. *J. Clin. Med.* 2020, 9, 191, doi:10.3390/jcm9010191.
6. Stortz, J.A.; Murphy, T.J.; Raymond, S.L.; Mira, J.C.; Ungaro, R.; Dirain, M.L.; Nacionales, D.C.; Loftus, T.J.; Wang, Z.; Ozrazgat-Baslanti, T.; et al. Evidence for Persistent Immune Suppression in Patients Who Develop Chronic Critical Illness After Sepsis. *SHOCK* 2018, 49, 249–258, doi:10.1097/shk.0000000000000981.
7. Rosenthal, M.D.; Moore, F.A. Persistent inflammatory, immunosuppressed, catabolic syndrome (PICS): A new phenotype of multiple organ failure. *J. Adv. Nutr. Hum. Metab.* 2015, 1, doi:10.14800/janhm.784.
8. Mira, J.C.; Cuschieri, J.; Ozrazgat-Baslanti, T.; Wang, Z.; Ghita, G.L.; Loftus, T.J.; Stortz, J.A.; Raymond, S.L.; Lanz, J.D.; Hennessy, L.V.; et al. The Epidemiology of Chronic Critical Illness

- After Severe Traumatic Injury at Two Level–One Trauma Centers*. *Crit. Care Med.* 2017, 45, 1989–1996, doi:10.1097/ccm.0000000000002697.
9. Stortz, J.A.; Mira, J.C.; Raymond, S.L.; Loftus, T.J.; Ozrazgat-Baslanti, T.; Wang, Z.; Ghita, G.L.; Leeuwenburgh, C.; Segal, M.S.; Bihorac, A.; et al. Benchmarking clinical outcomes and the immunocatabolic phenotype of chronic critical illness after sepsis in surgical intensive care unit patients. *J. Trauma Acute Care Surg.* 2018, 84, 342–349, doi:10.1097/ta.0000000000001758.
 10. Manz, M.G.; Boettcher, S. Emergency granulopoiesis. *Nat. Rev. Immunol.* 2014, 14, 302–14, doi:10.1038/nri3660.
 11. Gabrilovich, D.I.; Nagaraj, S. Myeloid-derived suppressor cells as regulators of the immune system. *Nat. Rev. Immunol.* 2009, 9, 162–174, doi:10.1038/nri2506.
 12. Mathias, B.; Delmas, A.L.; Ozrazgat-Baslanti, T.; Vanzant, E.L.; Szpila, B.E.; Mohr, A.M.; Moore, F.A.; Brakenridge, S.C.; Brumback, B.A.; Moldawer, L.L.; et al. Human Myeloid-derived Suppressor Cells are Associated With Chronic Immune Suppression After Severe Sepsis/Septic Shock. *Ann. Surg.* 2017, 265, 827–834, doi:10.1097/sla.0000000000001783.
 13. Cuenca, A.G.; Delano, M.J.; Kelly-Scumpia, K.M.; Moreno, C.; Scumpia, P.O.; LaFace, D.M.; Heyworth, P.G.; Efron, P.A.; Moldawer, L.L. A Paradoxical Role for Myeloid-Derived Suppressor Cells in Sepsis and Trauma. *Mol. Med.* 2010, 17, 281–292, doi:10.2119/molmed.2010.00178.
 14. Loftus, T.J.; Mohr, A.M.; Moldawer, L.L. Dysregulated myelopoiesis and hematopoietic function following acute physiologic insult. *Curr. Opin. Hematol.* 2018, 25, 37–43, doi:10.1097/moh.0000000000000395.
 15. Yamanouchi, S.; Kudo, D.; Yamada, M.; Miyagawa, N.; Furukawa, H.; Kushimoto, S. Plasma mitochondrial DNA levels in patients with trauma and severe sepsis: time course and the association with clinical status. *J. Crit. Care* 2013, 28, 1027–31, doi:10.1016/j.jcrc.2013.05.006.
 16. Timmermans, K.; Kox, M.; Scheffer, G.J.; Pickkers, P. Danger in the Intensive Care Unit: Damps in Critically Ill Patients. *SHOCK* 2016, 45, 108–116, doi:10.1097/shk.0000000000000506.
 17. Picca, A.; Lezza, A.M.S.; Leeuwenburgh, C.; Pesce, V.; Calvani, R.; Bossola, M.; Manes-Gravina, E.; Landi, F.; Bernabei, R.; Marzetti, E. Circulating Mitochondrial DNA at the Crossroads of Mitochondrial Dysfunction and Inflammation During Aging and Muscle Wasting Disorders. *Rejuvenation Res.* 2018, 21, 350–359, doi:10.1089/rej.2017.1989.
 18. Puthuchery, Z.A.; Rawal, J.; McPhail, M.; Connolly, B.; Ratnayake, G.; Chan, P.; Hopkinson, N.S.; Padhke, R.; Dew, T.; Sidhu, P.S.; et al. Acute Skeletal Muscle Wasting in Critical Illness. *JAMA* 2013, 310, 1591–1600, doi:10.1001/jama.2013.278481.
 19. Leijte, G.P.; Rimmelé, T.; Kox, M.; Bruse, N.; Monard, C.; Gossez, M.; Monneret, G.; Pickkers, P.; Venet, F. Monocytic HLA-DR expression kinetics in septic shock patients with different pathogens,

sites of infection and adverse outcomes. *Crit. Care Lond. Engl.* 2020, 24, 110, doi:10.1186/s13054-020-2830-x.

20. Landelle, C.; Lepape, A.; Voirin, N.; Tognet, E.; Venet, F.; Bohé, J.; Vanhems, P.; Monneret, G. Low monocyte human leukocyte antigen-DR is independently associated with nosocomial infections after septic shock. *Intensive Care Med.* 2010, 36, 1859–1866, doi:10.1007/s00134-010-1962-x.

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