

Clinical investigation of suicidal behavior – research on immunological mechanisms and the possibilities of risk assessment and prediction

Doctoral (PhD) Thesis

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1 The Neurobiological Background of Suicide

Suicide is a dynamic, multifactorial phenomenon and represents a major public health problem worldwide. However, the accurate prediction of suicidal behavior remains limited, which justifies the use of models that take into account not only psychosocial stressors but also genetic, epigenetic, neurobiological, cognitive, and immunological vulnerability factors.

The suicidal spectrum extends from suicidal ideation through suicide attempt to completed suicide. From a clinical perspective, it is particularly important to understand which factors facilitate the transition from suicidal thoughts to suicidal action. The risk of suicidal behavior is shaped by both population-level factors, such as access to healthcare, economic difficulties, media reporting, and the availability of lethal means, and individual-level factors. Individual risk factors include neuropsychiatric disorders, previous suicide attempt, familial aggregation, substance use, adverse childhood experiences, negative life events, chronic or terminal somatic illnesses, pain, and sleep disturbances. Psychiatric diagnosis alone does not sufficiently explain suicidal behavior, since the majority of individuals living with major psychiatric disorders do not die by suicide.

The stress–diathesis model is of central importance in understanding suicidal behavior. According to this model, suicidal acts result from the interaction between persistent, trait-like vulnerability and current, state-dependent precipitating factors. Distal risk factors — such as genetic predisposition, early-life adversity, chronic illness, and persistent psychosocial burden — may increase an individual’s vulnerability over the long term. Through epigenetic and gene-expression changes, these factors may modify the stress response, immune function, serotonergic and dopaminergic neurotransmission, and neuroplasticity-related processes. In contrast, proximal factors — such as acute psychiatric episodes or severe negative psychosocial life events — immediately precede the suicidal crisis and may act as specific precipitating events.

Based on genetic and epigenetic research, suicide risk is partly heritable and may exert its effect independently of the heritability of psychiatric disorders. The impact of genetic vulnerability may also be mediated through cognitive characteristics, impulsive-aggressive behavior, decision-making deficits, and altered stress responses. Environmental adversities, particularly early trauma, may induce persistent epigenetic changes in systems responsible for the stress response, neuroplasticity, and emotion regulation. In the long term, these changes may increase the risk of maladaptive coping and suicidal behavior.

Among psychological and neuropsychological factors, disturbances of executive functions, impaired inhibitory control, alterations in attentional control, biased information processing toward negative stimuli, decision-making difficulties, memory impairments, and overgeneral autobiographical memory are of particular relevance. Reduced inhibitory control may facilitate impulsive responses, while impaired decision-making may lead to maladaptive actions, especially under conditions of uncertainty. Some cognitive abnormalities may be interpreted primarily as persistent vulnerability factors, whereas others may serve as markers of the current suicidal state.

Neuroimaging studies have identified several structural and functional abnormalities underlying suicidal behavior. The prefrontal cortex plays a key role, and its structural and functional alterations together form a symptom cluster that is highly relevant to suicide risk, including disturbances of emotion regulation, such as increased negative and reduced positive affect; negative cognitive patterns, such as rumination and self-blame; and motivational deficits, including helplessness and anhedonia. The anterior cingulate cortex is involved in conflict monitoring and affective processing, and its abnormalities may be associated with both the severity and lethality of suicidal behavior. The amygdala and hippocampus, which play fundamental roles in threat detection and contextual memory processes, show significant structural and functional alterations in suicidal behavior.

Among systemic regulatory disturbances, abnormalities of neurotransmitter systems, the stress axis, and the immune system are particularly important. Dysfunction of the serotonergic system is one of the most consistently demonstrated neurobiological abnormalities in suicidal behavior: reduced serotonin transporter density and lower cerebrospinal fluid serotonin metabolite levels may be associated with disturbances in prefrontal control, emotion regulation, impulse control, and decision-making. This is clinically relevant because, although SSRI treatment may reduce suicide risk through the improvement of depressive and anxiety symptoms, a transient increase in risk may occur in certain vulnerable groups during the early phase of treatment; therefore, the role of the serotonergic system is complex and requires close clinical monitoring. The dopaminergic system may contribute to hopelessness and maladaptive decision-making through its role in reward processing, motivation, and executive functioning. An imbalance between excitatory glutamate and inhibitory GABA can be interpreted as part of impaired neuroplasticity, a concept further supported by the clinical relevance of rapid-acting therapeutic approaches targeting N-methyl-D-aspartate receptors, such as esketamine.

Dysfunction of the HPA axis, particularly increased cortisol secretion, may represent one potential biological correlate of suicidal behavior and of its more severe, recurrent forms. Early

trauma, familial loading, and repeated stress exposure may modify the cortisol response, thereby influencing an individual's stress tolerance and suicidal vulnerability.

Immunological mechanisms may also play a role in the development of suicidal behavior. The association between chronic inflammation and suicidal behavior may be mediated by several interrelated biological mechanisms, including changes in cytokine levels, elevation of C-reactive protein, microglial activation, and a shift in tryptophan–kynurenine metabolism. Changes in monoamine neurotransmitter systems and neurotrophic factor expression, together with dysregulation of the stress-response system, may induce cognitive and behavioral alterations that contribute to the emergence of suicidal behavior.

Contemporary models of suicidal behavior conceptualize suicide risk not as a static entity but as a dynamically changing phenomenon, in which persistent vulnerability factors and proximal, state-dependent processes jointly lead to the development of a suicidal crisis. Accordingly, research is increasingly focused on capturing the acute suicidal state, that is, on identifying short-term clinically and biologically relevant indicators that go beyond traditional distal risk factors. From this perspective, it is particularly important to investigate both the clinical phenomenology of suicidal crisis and the associated objectifiable biological markers, including peripheral inflammatory alterations, since both approaches may contribute to the recognition of acute and imminent risk. The combined analysis of clinical, cognitive, neurobiological, and immunological markers may contribute to more accurate recognition of short-term risk, targeted prevention, and the development of a more objective, precision-oriented approach in suicidology.

The two studies presented in the present dissertation represent two complementary approaches to identifying the acute suicidal state. The first study examines whether routinely available peripheral low-grade inflammatory parameters can detect objectifiable biological alterations associated with a recent suicide attempt, that is, with an acute suicidal state. In parallel, the second study analyzes the extent to which a brief clinical screening procedure based on the symptoms of suicidal crisis can capture the same acute risk on the basis of the patient's current psychological state. Thus, the common aim of the two studies is not merely to describe suicide risk in general, but to identify acute, short-term suicidal risk at multiple levels: on the one hand, by means of an easily accessible biological tool, and on the other, through a rapidly applicable clinical instrument.

2 Low-grade inflammatory parameters may be associated with recent suicide attempts – a naturalistic study among psychiatric inpatients with depressive disorders

2.1 Introduction

Recent research suggests that suicidal behavior may be associated with low-grade systemic inflammation, which may be reflected in alterations in peripheral blood count and inflammatory parameters. Studies in suicidal patients have reported changes in white blood cell, neutrophil, and monocyte counts, C-reactive protein levels, as well as in the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR). These parameters are advantageous because they can be assessed rapidly and at low cost as part of routine laboratory testing. Although previous findings are partly inconsistent due to methodological differences, increasing evidence supports an association between certain peripheral immunological parameters related to low-grade inflammation, major depressive disorder, and suicidal behavior. Therefore, we investigated whether a recent suicide attempt by medication overdose among psychiatric inpatients with depressive disorder was associated with routinely available laboratory parameters indicative of low-grade inflammation.

The main research questions were as follows:

1. Can differences in the immunological profile be detected between depressed patients who recently attempted suicide and depressed patients without a current suicide attempt?
2. Which peripheral immunological parameters related to low-grade inflammation show the strongest association with recent suicide attempt?
3. How do factors such as sex, age, lifetime suicide risk, and the severity of depressive symptoms influence immunological parameters in depressed inpatients?

2.2 Methods

The study population consisted of psychiatric inpatients treated for a depressive episode at the Department of Psychiatry and Psychotherapy, University of Pécs, between December 1, 2020 and December 31, 2021, with or without a current suicide attempt (N = 100). The sample included 36 patients who had recently attempted suicide and 64 individuals without a current suicide attempt, including patients with a history of previous suicide attempt but no attempt

during the study period. Patients hospitalized due to an acute suicide attempt were assigned to the recent suicide attempt group.

To ensure group homogeneity, only patients who had attempted suicide by medication overdose were included, thereby avoiding methods such as cutting, stabbing, jumping from a height, hanging, and others that could directly affect immunological and inflammatory parameters. Patients with current intense suicidal ideation or a suicide attempt within the preceding month were also excluded. The only exception was made for individuals who had attempted suicide within three days before admission, as they were assigned to the recent suicide attempt group. Additional exclusion criteria included acute infections, chronic immunological-rheumatological, musculoskeletal, or central nervous system diseases, as well as anti-inflammatory pharmacotherapy. Patients who had previously received specific immunological treatment or were receiving such therapy at the time of inclusion were also excluded from the study.

Participation in the study was voluntary, and all procedures were carried out after signing the informed consent form. Participants completed questionnaires and took part in a semi-structured interview. To ensure homogeneity, data collection in both groups was performed within three days of hospital admission or the suicide attempt.

Participation was offered to a total of 111 patients; 100 individuals took part in the study, while 11 declined participation. Participation or refusal to participate had no influence on the patients' clinical care.

Basic demographic data, depression severity, suicide risk, and immunological parameters were recorded, including white blood cell count with lymphocyte, monocyte, neutrophil, eosinophil, and basophil granulocyte counts, platelet count, and high-sensitivity C-reactive protein. Immunological parameters were determined on the day following admission as part of routine laboratory testing. Based on the laboratory results, the neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, and platelet-to-lymphocyte ratio were calculated.

The nine-item Patient Health Questionnaire (PHQ-9) and the Suicide Risk Assessment Scale (SRAS) were used to assess the severity of depression and lifetime suicide risk, respectively.

For the two participant groups (recent suicide attempters and non-recent suicide attempters), we conducted a descriptive analysis covering age, gender, scores derived from clinical questionnaires (PHQ-9, SRAS), and laboratory findings. To identify statistical differences between the groups, the Wilcoxon rank-sum test was used for continuous variables, while Pearson's chi-squared test and Fisher's exact test were applied to ordinal and categorical

variables. P-values were adjusted for multiple comparisons using the Benjamini–Hochberg false discovery rate (FDR) procedure.

Given the relatively small sample size and the non-normal distribution of several continuous variables, we consistently used non-parametric tests throughout the analysis to avoid assumptions of normality. No values were excluded or trimmed in order to retain statistical power and reflect real-world variability.

Logistic regression analyses were carried out on the binary variable representing suicide attempts, where '1' denoted individuals in the recent suicide attempter group and '0' represented those who had not attempted suicide recently (previously attempted suicide or never attempted suicide). A *p*-value below 0.05 was considered to indicate statistical significance.

2.3 Results

The most frequent primary diagnoses were single-episode major depressive disorder, recurrent major depressive disorder, mixed anxiety and depressive disorder, and depressive episode of bipolar affective disorder. Comorbid psychiatric disorder was present in 95 patients.

No statistically significant difference was observed between the recent suicide attempt group and the non-recent suicide attempt group in terms of age, sex, or depression severity as measured by the PHQ-9. Among the immunological parameters, the raw, uncorrected values of white blood cell count, neutrophil count, eosinophil count, monocyte count, as well as the NLR and MLR, were significantly higher in the recent suicide attempt group. However, after applying Benjamini–Hochberg false discovery rate correction for multiple comparisons, none of these differences remained statistically significant. No group difference was detected in CRP levels.

In each model, one inflammatory marker — platelet count, NLR, MLR, PLR, or CRP — was included as the main explanatory variable, while age, sex, continuous PHQ-9 total score, and dichotomized cumulative suicide risk were entered as covariates. Among the models, only the MLR proved to be an independent, statistically significant predictor of recent suicide attempt. The other examined markers showed no significant association with the outcome variable in the covariate-adjusted models.

To assess the robustness of the findings, a sensitivity analysis was performed, excluding currently depressed patients who reported a previous, but non-recent, suicide attempt in their history. In the restricted sample, the re-estimated logistic regression model showed an effect size of similar magnitude for the MLR; however, the association remained borderline significant. The odds ratio continued to indicate a large effect, although the wide confidence

interval reflected low precision of the estimate. None of the covariates proved statistically significant. Model fit was adequate, and the Hosmer–Lemeshow test indicated satisfactory calibration.

Strong, significant positive correlations were observed between the NLR and MLR, the NLR and PLR, and the PLR and MLR. CRP showed no significant correlation with other immunological parameters, except for eosinophil granulocyte count.

The immunological variables were analyzed in separate models in order to minimize multicollinearity resulting from substantial intercorrelations. No significant positive association was detected between depression severity and suicide risk; however, significant negative associations were observed between the PLR and depression, as well as between the NLR, MLR, and lifetime suicide risk.

2.4 Discussion

2.4.1 Interpretation of the Findings

In line with previous research, our results indicate that several peripheral markers suggestive of low-grade inflammation — white blood cell count, neutrophil granulocyte count, monocyte count, the neutrophil-to-lymphocyte ratio, and the monocyte-to-lymphocyte ratio — were higher among depressed patients who had made a current suicide attempt than among those without a recent attempt. However, these differences did not reach statistical significance. Regression analysis, nevertheless, showed that the MLR remained significantly elevated in the recent suicide attempt group after adjustment for covariates, including age, sex, lifetime suicide risk, and depression severity. Our findings suggest that the combined elevation of peripheral immune parameters may be associated with an acute suicide attempt and may reflect the presence of a low-intensity, nonspecific, complex immunological mechanism. At the same time, these findings should be regarded as exploratory and cannot be considered definitive evidence for low-grade inflammatory biomarkers related to suicidality.

CRP levels were also higher among patients with a recent suicide attempt; however, the difference was not statistically significant. Our findings do not clearly support previous observations that identified eosinophil count and CRP as potential biomarkers of suicidal behavior. This observation may also be interpreted as suggesting that elevated CRP levels are more closely related to more severe forms of mood disorders, or to a potential inflammatory subtype of these disorders, rather than directly to suicidal behavior. In contrast, our results

suggest that markers reflecting cellular immunity, such as the NLR and MLR, may show a more specific association with recent suicide attempt.

In our study, CRP did not show a significant correlation with other immunological parameters, except for eosinophil granulocyte count, which may indicate the presence of a potentially distinct regulatory pathway and warrants further investigation.

A particularly noteworthy finding is that the examined peripheral immunological parameters showed negative associations with depression severity and lifetime suicide risk. These results suggest that immunological alterations associated with suicidal behavior may be partly independent of depression severity, and may also indicate a specific subgroup of depressed patients characterized by increased immune activation.

Overall, our findings are consistent with previous observations suggesting that patients with recent suicide attempts — in whom several markers related to low-grade inflammation are concurrently elevated — may represent a potentially distinguishable subgroup within the depressed population. In this subgroup, immunological alterations may be more likely to contribute to the underlying depression, and suicide risk may also be higher.

2.4.2 Strengths and Limitations

The main limitations of the study include its cross-sectional design and relatively small sample size, which provide only a snapshot of the current psychological and neurobiological state of depressed patients. This limits the possibility of drawing causal conclusions regarding the relationship between suicidal behavior and low-grade inflammation. A further limitation is the relatively low number of participants in both the recent suicide attempt and non-recent suicide attempt groups, although clinically relevant immunological differences were detectable despite the small sample size. Another limitation is that the study did not include a healthy, non-depressed control group.

One of the strengths of the study is its naturalistic methodology and the broad assessment of routinely measurable immunological parameters. The exclusion of acute and chronic inflammatory conditions, immunological diseases, and relevant treatments, together with the restriction of the sample to attempts by medication overdose, reduced the potential bias caused by infections, somatic illnesses, medication effects, and tissue injuries associated with violent methods.

The reliability of the results is strengthened by the fact that age, sex, depression severity, and lifetime suicide risk were controlled for in the statistical models. In addition, the study focused on depressed patients receiving psychiatric inpatient care, who represent a particularly high-

risk population with regard to suicidal behavior; therefore, the findings may provide valuable clinical, real-world observations.

2.5 Conclusions

Despite the relatively small sample size and other methodological limitations, our findings suggest a statistically non-significant association between certain immunological parameters related to low-grade inflammation — particularly the NLR and MLR — and recent suicide attempt by medication overdose among depressed inpatients. These inflammatory parameters showed negative correlations with depression severity and lifetime suicide risk. Our results suggest that immunological mechanisms may potentially contribute to the development of current suicide attempts, independently of the underlying psychiatric disorders. The combined elevation of immunological parameters — independently of depression severity — may indicate psycho-neuro-immunological alterations associated with recent suicide attempt, rather than serving as an indicator of lifetime suicide risk. At present, there are no widely accepted, evidence-based guidelines for the routine screening or treatment of suicidal behavior — even in high-risk groups — based on the immunological theory of suicide, including interventions such as anti-inflammatory medication.

3 Assessment of Acute Suicide Risk – Possibilities of Complex Risk Assessment in Clinical Practice

3.1 Introduction

The recognition of acute suicide risk is of paramount importance for the prevention of suicidal behavior; therefore, one of the major aims of contemporary suicidological research is to identify more precisely the characteristics of the psychological process leading to suicidal acts. Despite intensive research efforts, data that would allow the accurate and reliable assessment of the presuicidal mental state and acute suicide risk remain limited. Traditional risk assessment instruments primarily measure static factors and are therefore limited in the evaluation of imminent risk. Another central component of risk assessment is the identification of suicidal thoughts and intentions. However, these often do not help to predict suicidal acts, as they are variable and may be present even in the absence of imminent suicide risk.

Taking these limitations into account, research aimed at the more accurate assessment of the presuicidal mental state has led to the development of suicide-specific syndromes describing the mental state preceding suicide. The newly described suicide-specific symptom clusters include Acute Suicidal Affective Disturbance (ASAD) and Suicide Crisis Syndrome (SCS). The latter describes a presuicidal mental state characterized by affective and cognitive dysregulation, encompassing cognitive and emotional responses to real or perceived threat. The core symptoms of Suicide Crisis Syndrome include a persistent or recurrent feeling of being trapped in an intolerable situation, from which the individual feels unable either to cope or to escape. Additional important features include associated affective symptoms, such as depression, despair, panic-like anxiety, psychological pain, and acutely developing anhedonia; loss of control over cognitive processes, including rumination, cognitive rigidity and constriction, and attempts to suppress negative thoughts; narrowing of problem-solving capacity; and changes associated with increased arousal, such as agitation, hypervigilance, irritability, and insomnia. This concept also emphasizes that symptoms develop rapidly and persist or recur over time. Another important feature is that the presence of suicidal thoughts or intentions is not necessarily required for the diagnosis of Suicide Crisis Syndrome. Several screening and diagnostic questionnaires have been developed to identify symptoms of Suicide Crisis Syndrome, including the SCI, SCI-2, SCI-SF, SCS-C, and A-SCS-C. These instruments contain questions assessing the most important symptoms of the syndrome, including entrapment, panic-dissociation, ruminative thinking, emotional pain, and fear of death. Their

internal consistency, validity, and predictive significance have been demonstrated in several studies, and the entrapment subscale has been shown to be of particular importance.

A brief screening test developed on the basis of the symptoms of Suicide Crisis Syndrome may provide more reliable support in emergency care for the rapid and accurate assessment of acute suicide risk and for selecting the appropriate level of care than the assessment of suicidal ideation alone.

Based on previous studies, we designed our research to perform the Hungarian adaptation of the suicide risk screening test used by Galynker and colleagues and to examine its clinical applicability.

3.2 Method

Data were collected consecutively from all patients who received outpatient or inpatient care at the Department of Psychiatry and Psychotherapy, University of Pécs, between October 9 and 31, 2023. The screening questionnaire was administered to all patients seeking immediate help, except for those whose cooperation was limited due to impaired consciousness, severe behavioral disturbance, such as psychotic, aggressive, or agitated states, or severe dementia.

In patients admitted to the ward, the questionnaires were also administered at discharge. The method used in our study was developed on the basis of the screening test applied by Galynker and colleagues in emergency care. Accordingly, the brief Acute Suicide Risk Test (ASRT) was used to assess current crisis symptoms.

In addition, the Suicide Risk Assessment Scale (SRAS), developed by Rihmer and colleagues, was administered to identify the most important general suicide risk factors. Of the five items of the ASRT, the first two questions, corresponding to the A-SCS-C, assess the core symptoms of acute suicidal crisis, namely entrapment and overwhelming, uncontrollable negative thoughts. The other three items are derived from the widely used Columbia-Suicide Severity Rating Scale (C-SSRS) and assess indirect suicidal intentions, direct suicidal thoughts, and preparatory behaviors.

The items of the Rihmer SRAS include weighted questions regarding the most important general suicide risk factors. In cases where any of these screening instruments, the ASRT or the SRAS, indicated suicide risk, the more detailed diagnostic questionnaire assessing the symptoms of Suicide Crisis Syndrome, the Suicide Crisis Syndrome Checklist (SCS-C), was administered in the form of a semi-structured interview.

Based on the result of the SCS-C, it can be determined whether: 1) Suicide Crisis Syndrome is not present; 2) Suicide Crisis Syndrome is present; or 3) severe Suicide Crisis Syndrome is present.

3.3 Results

During the study period between October 9 and 31, 2023, a total of 150 questionnaires were completed by 99 patients. One-third of the patients ($n = 35$) received outpatient care, while two-thirds ($n = 64$) received inpatient care. Among the 64 patients admitted to the ward, the tests were also administered at discharge in 51 cases.

The most frequent leading clinical diagnoses were depressive disorders (44.7%), adjustment disorders (34%), psychotic disorders (33.3%), and substance use disorders (33.3%). The rate of comorbidity was high, with nearly half of the patients receiving more than one psychiatric diagnosis.

The screening tests (ASRT, SRAS) indicated suicide risk in more than half of the patients receiving outpatient care and in three-quarters of those admitted to inpatient care. Following inpatient treatment, among the 51 patients who also completed the tests at discharge, this proportion decreased to only one-third.

Among patients admitted to the ward, only the ASRT was positive in one-quarter of cases, while only the general risk assessment questionnaire (SRAS) was positive in 14% of cases; concurrent positivity of both instruments was confirmed in more than one-third of patients. Based on these findings, neither the ASRT nor the SRAS alone determined inpatient admission; however, when both instruments were positive, psychiatric hospitalization was the most frequent form of care. When examining the associations between suicide risk assessment and the symptoms of Suicide Crisis Syndrome, we aimed to determine how positivity on the brief screening tests (ASRT, SRAS) was related to the results of the detailed Suicide Crisis Syndrome diagnostic scale (SCS-C), that is, the predictive value of each screening test for the full symptom spectrum of Suicide Crisis Syndrome. Positivity on the detailed SCS-C was most frequent among those for whom the 2 + 3-item screening test assessing the acute mental state ($ASRT = A-SCS-C + C-SSRS$) was also positive, either alone or together with the SRAS. Severe Suicide Crisis Syndrome symptomatology occurred most frequently when both the ASRT and the SRAS were positive. Separate analysis of the two components of the ASRT also showed that symptoms of Suicide Crisis Syndrome were most frequent among those in whom the two A-SCS-C screening questions — entrapment and negative thoughts — indicated suicide risk, whereas this proportion was only 28.6% for the three C-SSRS questions. The SRAS alone showed little

association with symptoms of Suicide Crisis Syndrome. For the two-item screening test (A-SCS-C), the rate of false-positive cases in relation to the detailed SCS-C was 12.7% (7/55), while the rate of false-negative cases was 22.7% (5/22). Based on these results, the sensitivity of the two-item screening test for the clinical state of Suicide Crisis Syndrome was 90.1, and its specificity was 70.1.

3.4 Discussion

Similar to previous international findings, our Hungarian study confirmed the clinical applicability of a suicide risk screening test based on the SCS concept. The two questions assessing the core symptoms of Suicide Crisis Syndrome identified current suicide risk in a substantial proportion of cases, whereas the presence of direct suicidal thoughts — although useful in everyday clinical practice for recognizing suicide risk — was less indicative of an acute suicidal crisis. Our results confirmed one of the greatest advantages of this screening method: it enables the recognition of potential suicide risk even when the patient does not report direct suicidal intentions. The screening test comprising the two core symptoms of suicidal crisis was associated with the full symptom spectrum of Suicide Crisis Syndrome with high sensitivity and somewhat lower specificity. This finding suggests that the presuicidal mental state associated with acute suicide risk can be identified with a high degree of certainty using the two screening questions.

In our view, this simple screening method, which can be easily applied in everyday clinical practice, has important implications for suicide prevention, as it provides substantial support in the accurate assessment of the patient's current psychological state, even in cases where direct suicidal thoughts or intent do not emerge. In addition, both the brief and the full screening instruments proved to be independent predictors of inpatient admission, even after taking clinical, demographic, and suicide-specific risk factors into account. The present study contributes to the international literature by demonstrating the clinical utility of the instrument in a real-world psychiatric clinical setting. Its clinical application supports decision-making in acute care, reduces the risk of underestimation and overestimation, and contributes to the appropriate timing of treatment.

3.5 Conclusion

The use of the described screening tests may be particularly helpful in emergency departments and acute psychiatric care, while they may also be effectively applied in follow-up care, chronic psychiatric care, and other medical specialties. Given that these questionnaires are simple and

quick to administer and easy to evaluate, we hope that their use will become more widespread in Hungary and contribute to effective suicide prevention practice.

Beyond their clinical significance, these tests may also serve as useful reference points as part of medical documentation in ethical, insurance-related, or legal matters. Based on the promising preliminary findings, we plan to conduct a larger-sample longitudinal study over a longer period in order to evaluate more precisely the clinical applicability and predictive validity of the suicide risk assessment scale.

4 Summary and Conclusions

Based on our findings, the clinical assessment of suicide risk cannot rely exclusively on static, general, or lifetime risk factors. Although these are important for understanding suicidal vulnerability, the recognition of acute risk also requires state-sensitive methods capable of capturing short-term clinically and biologically relevant changes.

The first original study of the dissertation suggests that low-grade inflammatory parameters may represent biological correlates of recent suicide attempt; however, in their current form, they cannot yet be considered independent, routinely applicable clinical biomarkers. Their clinical value lies rather in their potential contribution to a more objective psycho-neuro-immunological interpretation of the acute suicidal state, and they may later become valuable components of a complex, multivariable risk assessment model.

Based on the results of the second study, brief screening instruments based on the symptoms of suicidal crisis may provide promising support in acute psychiatric and emergency care. The study suggests that assessing entrapment and uncontrollable negative thoughts may bring clinicians closer to identifying the actual presuicidal mental state than approaches focusing exclusively on direct suicidal ideation or general risk factors. This is particularly important in cases where, for various reasons, the patient does not openly report suicidal intent.

Taken together, the two studies support the view that future suicide prevention research and clinical practice should move toward a multimodal, state-sensitive approach. Further progress requires larger-sample, prospective, longitudinal studies that simultaneously examine the short-term predictive value of biological and clinical variables.

Further studies related to both research directions of the present dissertation are currently ongoing, partly within international collaborations. The aim of the immunological studies is to characterize more precisely the inflammatory mechanisms associated with suicidal behavior by examining more specific markers, such as IL-22, TNF- α , IL-6, IL-10, and osteopontin. Data collection for the clinical screening of acute suicide risk has been extended to a six-month period in order to increase the sample size, and data processing is currently ongoing. The aim of these further studies is to determine how the combined analysis of clinical state markers and immunological parameters may contribute to the more accurate recognition of acute suicide risk and to the development of more state-sensitive risk assessment models, thereby ultimately contributing to the reduction of suicide mortality.

5 Novel Findings of the Dissertation

- Among depressed inpatients, immunological parameters associated with low-grade inflammation, particularly the NLR and MLR, showed a tendency toward higher values in patients with a recent suicide attempt by medication overdose; however, this association did not reach statistical significance.
- The examined immunological parameters showed negative associations with depression severity (PLR) and lifetime suicide risk (NLR, MLR), suggesting that immunological alterations associated with suicidal behavior may be partly independent of depression severity and may also indicate a specific subgroup of depressed patients characterized by increased immune activation.
- The brief screening test assessing the two core symptoms of suicidal crisis (A-SCS-C) identified the full symptom spectrum of Suicide Crisis Syndrome with high sensitivity, while its diagnostic value and specificity were further increased when used in combination with the RSzK, which also assesses lifetime suicide risk.
- The SCS screening test enables the recognition of suicide risk even when the patient does not report suicidal intentions.
- The brief SCS screening test may be particularly useful in emergency departments, while the detailed diagnostic instrument may provide additional support in specialized psychiatric care.

6 Publications

6.1 Publications Related to the Thesis

Lovig, C. , Osvath, P., Saghy, E., Molnar, C., Kovacs, M. A., Petho, B., Simon, D., Fekete, S., Tenyi, T., Voros, V. (2026). Low-grade inflammatory parameters may be associated with recent suicide attempts—A naturalistic study among psychiatric inpatients with depressive disorders. *Frontiers in Psychiatry*, 17, 1707768. *Impact factor: 3.2*

Osváth, P., Molnár, C., Lovig, C. , Major, F. N., Venczák, S., Fekete, S., Tényi, T., Cohen, L., Galynger, I., Vörös, V. (2025). Assessment of acute suicide risk. *Orvosi Hetilap*, 166(4), 146–153. *Impact factor: 0.9*

6.2 Oral and Poster Presentations Related to the Thesis

28th Annual Meeting of the Hungarian Psychiatric Association, Siófok, January 29 – February 1, 2025 – oral presentation in Hungarian: “New Possibilities for the Recognition of Acute Suicide Risk – Suicide Crisis Syndrome in Clinical Practice”

34th European Congress of Psychiatry, Prague, March 28–31, 2026 – e-poster viewing in English: “Implementation and Clinical Utility of Suicide Crisis Syndrome Screening in an Acute Psychiatric Setting: A Prospective Observational Study”

6.3 Thesis-Related Abstracts Published in Scientific Journals

Major, F. N.; Vörös, V.; Venczák, Sz.; Lovig, Cs.; Pethő, B.; Molnár, Cs.; Kovács, M. Á.; Fekete, S.; Tényi, T.; Osváth, P. (2026). The immunological background of suicide attempts. *Psychiatria Hungarica*, 41, Suppl. 1, p. 122.

6.4 Publications Not Directly Related to the Thesis

Lengyel, Z., Lovig, C., Kommedal, S., Keszthelyi, R., Szekeres, G., Battyáni, Z., Csernus, V., Nagy, A. D. (2013). Altered expression patterns of clock gene mRNAs and clock proteins in human skin tumors. *Tumor Biology*, 34(2), 811–819. *Impact factor: 3.6*

Lovadi, E., Csécei, P., Lovig, C., Karádi, Z., Szapáry, L. (2016). Lipids and cerebrovascular disease-New therapeutic options in lowering LDL-cholesterol. *Orvosi Hetilap*, 157(52), 2059–2065.

Impact factor: 0.9

Karadi, Z. N., Csecsei, P., Lovig, C., Lovadi, E. I., Szapary, L. (2016). The Clinical Relevance of Cerebral Microbleeds. *International Journal of Clinical Therapeutics and Diagnosis*, 4(4), 124–133.

Impact factor: 6.3

Lovig, C., Herold, R., Pál, E., Bóné, B., Faludi, B., Albert, N., Dibusz, D., Hernádi, G., Péterfi, Z., Sipos, D., Tényi, T. (2024). Progressive multifocal leukoencephalopathy associated with AIDS diagnosed in a psychiatric department. *Orvosi Hetilap*, 165(33), 1295–1302.

Impact factor: 0.9

Tényi, T., Lovig, C., & Pethő, B. (2025). Jean Marie Joseph Capgras (1873–1950) – 75 years since the death of the describer of the delusion of doubles. *Orvosi Hetilap*, 166(11), 434–438.

Impact factor: 0.9

Impact factor of scientific publications related to the thesis: 4.1

Total impact factor of all scientific publications, excluding abstracts: 16.7

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